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=> d his

     (FILE 'HOME' ENTERED AT 15:30:47 ON 09 JAN 2003)

     FILE 'REGISTRY' ENTERED AT 15:30:52 ON 09 JAN 2003
L1             0 S NOMEGESTEROL ACETATE
L2             1 S NOMEGESTROL ACETATE

     FILE 'REGISTRY' ENTERED AT 15:32:41 ON 09 JAN 2003
L3             0 S L1
L4             1 S L2

     FILE 'CAPLUS' ENTERED AT 15:34:27 ON 09 JAN 2003
L5            78 S L4
L6            78 S L2
L7            22 S L6 AND ESTROGEN
L8             9 S L7 AND TREATMENT
L9             1 S L7 AND POST MENOPAUSE
L10            5 S L7 AND CARDIOVASCULAR
L11            2 S L7 AND BLEEDING

=> s l5 and estradiol
          65609 ESTRADIOL
L12          30 L5 AND ESTRADIOL

=> s l12 and post menopause
         155979 POST
           8188 MENOPAUSE
             75 POST MENOPAUSE
                (POST(W)MENOPAUSE)
L13           1 L12 AND POST MENOPAUSE

=> s l12 and harmone replacement
             13 HARMONE
          97742 REPLACEMENT
              0 HARMONE REPLACEMENT
                (HARMONE(W)REPLACEMENT)
L14           0 L12 AND HARMONE REPLACEMENT

=> d l13

L13  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2003 ACS
AN   2001:566988  CAPLUS
DN   135:327515
TI   Withdrawal of hormone replacement therapy is associated with significant
     vertebral bone loss in postmenopausal women
AU   Tremollieres, F. A.; Pouilles, J.-M.; Ribot, C.
CS   Menopause and Bone Metabolic Disease Unit, CHU Rangueil, Toulouse,
     F-31403, Fr.
SO   Osteoporosis International (2001), 12(5), 385-390
     CODEN: OSINEP; ISSN: 0937-941X
PB   Springer-Verlag London Ltd.
DT   Journal
LA   English
RE.CNT  20    THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
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=> s estrogenic deficiencies
         14043 ESTROGENIC
         18361 DEFICIENCIES
L15          3 ESTROGENIC DEFICIENCIES
                (ESTROGENIC(W)DEFICIENCIES)

=> d l15 1-3 ibib hitstr abs

L15  ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         1998:239116  CAPLUS
DOCUMENT NUMBER:          128:312905
TITLE:                    Pharmaceutical composition consisting of an estrogen
                          and a progestogen
INVENTOR(S):              Lanquetin, Michel; Paris, Jacques; Thomas, Jean-Louis
PATENT ASSIGNEE(S):       Laboratoire Theramex, Monaco; Lanquetin, Michel;
                          Paris, Jacques; Thomas, Jean-Louis
SOURCE:                   PCT Int. Appl., 22 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 French
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 9815279         A1   19980416       WO 1997-FR1792   19971008
         W:  AU, BR, CA, CN, CU, CZ, HU, ID, IL, JP, KR, MG, MX, NO, NZ, PL,
             RO, RU, SG, SK, TR, US, VN, YU
         RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
             GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
             GN, ML, MR, NE, SN, TD, TG
     FR 2754179         A1   19980410       FR 1996-12239    19961008
     FR 2754179         B1   19981224
     AU 9746273         A1   19980505       AU 1997-46273    19971008
     AU 745571          B2   20020321
     ZA 9709011         A    19980603       ZA 1997-9011     19971008
     BR 9712274         A    19990831       BR 1997-12274    19971008
     EP 956022          A1   19991117       EP 1997-944940   19971008
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
     CN 1239893         A    19991229       CN 1997-180380   19971008
     JP 2002509524      T2   20020326       JP 1998-517263   19971008
     NO 9901593         A    19990607       NO 1999-1593     19990331
     MX 9903291         A    20000131       MX 1999-3291     19990408
     KR 2000048981      A    20000725       KR 1999-703032   19990408
PRIORITY APPLN. INFO.:                   FR 1996-12239    A  19961008
                                         WO 1997-FR1792   W  19971008
AB   The invention concerns the field of chem. therapy and more particularly
     the field of pharmaceutical hormonal technique.  More precisely it
     concerns novel pharmaceutical hormonal compns. characterized in that they
     are formed by an estrogen-progestogen combination assocd. or mixed with 1
     or several nontoxic, inert and excipients, for oral administration.  The
     combined assocn. can be prescribed continuously or intermittently, for
     producing a compn. for treating estrogenic deficiencies
     , preventing osteoporosis and cardiovascular diseases in menopausal women,
     or still for blocking ovulation in a woman during the period of ovarian
     activity.  Thus, tablets contained estradiol 1.5, nomegestrol acetate 2.5,
     Avicel PH-102 22.4, lactose 60, PVP 8.4, colloidal silica 1.2, glycerol
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palmitostearate 3.6, and dye 0.4 mg. The effectiveness of this combination in the treatment of diseases in menopausal women was demonstrated.

L15 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1971:463433 CAPLUS
DOCUMENT NUMBER: 75:63433
TITLE: Benzoic acid lactones and their intermediates
INVENTOR(S): Cross, Alexander D.; Fried, John H.; Harrison, Ian T.
PATENT ASSIGNEE(S): Syntex Corp.
SOURCE: U.S., 7 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3585216	A	19710615	US 1966-566204	19660719

PRIORITY APPLN. INFO.: US 1966-566204 19660719
GI For diagram(s), see printed CA Issue.
AB An example of the title lactones, useful in treatment of **estrogenic deficiencies**, is 2-(6-oxo-10-hydroxyundec-1-enyl)-4,6-dihydroxybenzoic acid 10-lactone (I). This compd. is prepd. by dietherification of 2,4,6-Me(OH)2C6H2CO2Et with dihydropyran to give the ester II (Y = CO2Et, Z = Me), reduced with LiAlH4 in THF to the corresponding alc. II (Y = CH2OH, Z = Me). The carbinol and MeCHBrCH2CH2CO2Et stirred 24 hr at 20.degree. in DMF in the presence of Ag2O and the mixt. dild. with CHCl3 gave II (Y = CH2OCHMeCH2CH2CO2Et, Z = Me). This product oxidized by CrO3 in 1:1 AcOH-Ac2O and the diacetoxymethyl deriv. submitted to mild base hydrolysis yielded the corresponding aldehyde II (Y = CH2OCHMeCH2CH2CO2Et, Z = CHO). Condensation of the aldehyde with the Ph3P adduct of Cl(CH2)4CO2Et gave the diester II (Y = CH2OCHMeCH2CH2CO2Et, Z = CH:CHCH2CH2CH2CO2Et), cyclized by treatment with Na in xylene to give a mixt. of the 6-oxo-7-hydroxy and 6-hydroxy-7-oxo cyclic acyloin derivs. (III). Submission of III to a sequence involving standard acetylation, treatment with Zn dust in AcOH, standard acetylation and subsequent acylation gave the corresponding 4,6-diacyloxy compd. IV (R = Ac, X = H2). Protection of the nonaromatic double bond unsatn. by bromination, oxidn. with CrO3-AcOH or RuO4 in CH2Cl2, and debromination with Zn dust in AcOH gave IV (R = Ac, X = O) converted by basic hydrolysis to I.

L15 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1967:408394 CAPLUS
DOCUMENT NUMBER: 67:8394
TITLE: The test of testosterone in **estrogenic deficiencies**
AUTHOR(S): Ciocirdia, Cezarina; Serban, Al. M. D.; Stroe, Emilia; Bunea, Minodora
CORPORATE SOURCE: Acad. Rep.Socialiste Roumaine, Bucharest, Rom.
SOURCE: Revue Roumaine d'Endocrinologie (1967), 4(1), 63-70
CODEN: RRENAR; ISSN: 0035-4015
DOCUMENT TYPE: Journal
LANGUAGE: French
AB Metabolism of exogenous testosterone has been studied with ovariectomized women. To 6 woman a dose of 75 mg. testosterone propionate was administered. The ratio of androsterone (I) to etiocholanolone (II) is

diminished, due to an augmentation of the II in basal conditions as well as after treatment. Estrogen levels are lowered before and augmented after the treatment. Estrogens appear to affect the metabolism of androgens, with an orientation to I due to activation of the 5.alpha.-reductase. Deficiency of estrogens det. metabolism to II.

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     (FILE 'HOME' ENTERED AT 15:30:47 ON 09 JAN 2003)

     FILE 'REGISTRY' ENTERED AT 15:30:52 ON 09 JAN 2003
L1            0 S NOMEGESTEROL ACETATE
L2            1 S NOMEGESTROL ACETATE

     FILE 'REGISTRY' ENTERED AT 15:32:41 ON 09 JAN 2003
L3            0 S L1
L4            1 S L2

     FILE 'CAPLUS' ENTERED AT 15:34:27 ON 09 JAN 2003
L5           78 S L4
L6           78 S L2
L7           22 S L6 AND ESTROGEN
L8            9 S L7 AND TREATMENT
L9            1 S L7 AND POST MENOPAUSE
L10           5 S L7 AND CARDIOVASCULAR
L11           2 S L7 AND BLEEDING
L12          30 S L5 AND ESTRADIOL
L13           1 S L12 AND POST MENOPAUSE
L14           0 S L12 AND HARMONE REPLACEMENT
L15           3 S ESTROGENIC DEFICIENCIES

=> s l5 and estradiol
         65609 ESTRADIOL
L16         30 L5 AND ESTRADIOL

=> s l5 and women
         70337 WOMEN
L17         32 L5 AND WOMEN

=> s l17 and contraception
          2595 CONTRACEPTION
L18          7 L17 AND CONTRACEPTION

=> s l5 and menopause
          8188 MENOPAUSE
L19         17 L5 AND MENOPAUSE

=> s l19 and estrogen
         60689 ESTROGEN
L20         11 L19 AND ESTROGEN

=> d l19 1-11 ibib hitstr abs

L19  ANSWER 1 OF 17  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:        2002:859068  CAPLUS
DOCUMENT NUMBER:         137:362854
TITLE:                   Simvastatin, transdermal patch, and oral
                         estrogen-progestogen preparation in
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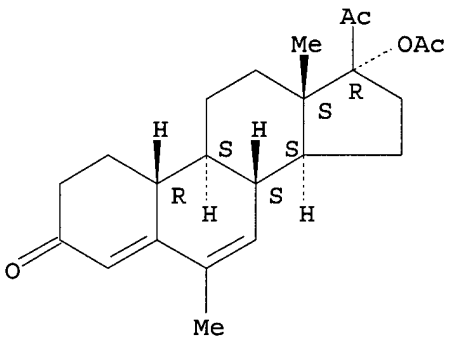
early-postmenopausal hypercholesterolemic women: a randomized, placebo-controlled clinical trial
AUTHOR(S): Vigna, Giovanni B.; Donega, Paola; Zanca, Rosanna; Barban, Angela; Passaro, Angelina; Pansini, Francesco; Bonaccorsi, Gloria; Mollica, Gioacchino; Fellin, Renato
CORPORATE SOURCE: Department of Clinical and Experimental Medicine, Section of Internal Medicine II, University of Ferrara, Ferrara, 44100, Italy
SOURCE: Metabolism, Clinical and Experimental (2002), 51(11), 1463-1470
CODEN: METAAJ; ISSN: 0026-0495
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **58652-20-3**, Nomegestrol acetate
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(simvastatin transdermal patch and oral estrogen-progestogen prepn. in early-postmenopausal hypercholesterolemic women)

RN 58652-20-3 CAPLUS

CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Hormone replacement therapy (HRT) seems to have a favorable influence on the plasma lipid profile. Only a few investigations have examd. the effects of HRT vs. hepatic hydroxymethyl glutaryl CoA (HMG-CoA) reductase inhibitors. We compared the relative effects of different hypolipidemic strategies on lipoproteins and coagulative parameters in women with recent-onset spontaneous **menopause**. In this 24-wk, placebo-controlled trial, 60 consecutive healthy women aged .gtoreq. 45 yr, with amenorrhea from 6 to 60 mo (mean, 1.9.+-.1.4 yr), serum FSH greater than 40 U/L, and slight to moderate hypercholesterolemia (low-d. lipoprotein-cholesterol [LDL-C] 160 to 250 mg/dL, high-d. lipoprotein-cholesterol [HDL-C] < 75 mg/dL, and triglycerides < 200 mg/dL) were enrolled and randomized to dietetic advice (placebo group), simvastatin 10 mg, 0.625 mg of conjugated equine estrogen (CEE), or 50 .mu.g estrogen transdermal patch (ETP). In the latter 2 cases, the progestative nomegestrol was added to estrogens (days 17 to 28 of the cycle). Lipoprotein parameters were evaluated after sepg. very-low-d. lipoproteins (VLDLs) by ultracentrifugation, while fasting glucose and insulin, homocysteine, and hemo-coagulative parameters were detd. in plasma. Fifty-four patients completed the trial. Total cholesterol (TC)

and LDL-C significantly decreased in the simvastatin (-62 mg/dL [-20%] and -72 mg/dL [-30%], resp.), CEE (-42 mg/dL [-13%] and -45 mg/dL [-18%]), and ETP (-30 mg/dL [-10%] and -26 mg/dL [-11%]) groups compared to baseline, but only simvastatin showed an effect significantly superior to diet alone. Apolipoprotein (Apo) B was decreased by simvastatin (-25%, P <.001) and by CEE (-10%, P <.05); again, simvastatin was more effective than either diet or ETP. Triglyceride concn. and VLDL-C were unmodified by treatments. HDL-C and Apo A-I significantly increased in the simvastatin group (+18% and +8%, resp.), while HDL-C was unmodified by both HRT regimens and Apo A-I was reduced by ETP treatment (-17%); lipoprotein[a] (Lp[a]) was decreased by both HRTs (-38%, P <.05, and -22%, P =.07, for CEE and ETP, resp.). Among coagulative parameters, plasminogen activator inhibitor-1 (PAI-1) was significantly reduced by CEE (-29%, P <.05) but not ETP treatment (+16%, P = not significant), while fibrinogen, antithrombin, and homocysteine were unaffected by therapy. Thus, HRT, particularly CEE, seems well tolerated and moderately effective in improving the lipid pattern and, perhaps, the coagulative/fibrinolytic balance in postmenopausal hypercholesterolemic women; it may represent a therapeutic option in slightly dyslipidemic subjects. Statins are preferred in case of more severe disease.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:832625 CAPLUS
DOCUMENT NUMBER: 137:316114
TITLE: Novel hormone composition comprising a estrogen compound and a gestagenic compound
INVENTOR(S): Paris, Jacques; Thomas, Jean-Louis
PATENT ASSIGNEE(S): Laboratoire Theramex, Monaco
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

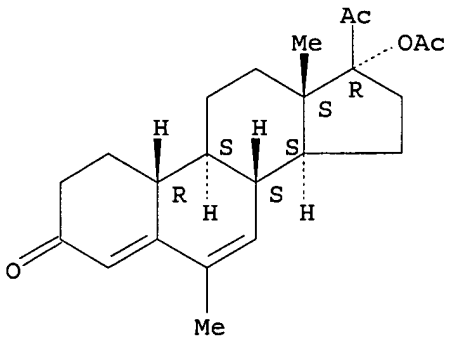
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085375	A1	20021031	WO 2002-FR1384	20020423
W: AE, AL, AU, BA, BG, BR, CA, CN, CO, CR, CU, CZ, DZ, EC, EE, HR, HU, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, RO, SG, SI, TN, US, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
FR 2823976	A1	20021031	FR 2001-5557	20010425

PRIORITY APPLN. INFO.: FR 2001-5557 A 20010425

IT **58652-20-3**, Nomegestrol acetate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel hormone compn. comprising estrogen compd. and gestagenic compd.)

RN 58652-20-3 CAPLUS
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

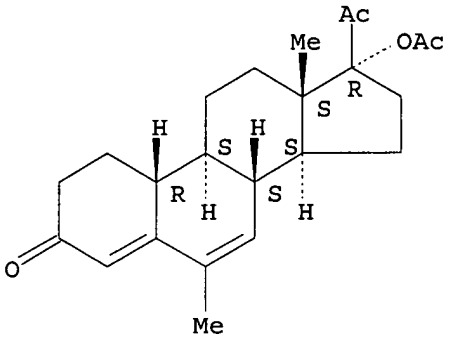


AB The invention relates to the field of therapeutic chem., more specifically to hormonal pharmaceutical techniques, esp. to novel hormonal pharmaceutical compns. which are formed as a result of an estro-gestagenic assocn. consisting of an estrogen compd. and a gestagenic compd., assocd. with or mixed with one or several non-toxic excipients which are inert and pharmaceutically acceptable and which can be administered orally. The invention also relates to the use of an estro-gestagenic mixt. wherein the estrogenic component and the gestagenic component are administered in a combined manner. Combined assocn. can be prescribed in a continuous or intermittent manner with a view to providing a compn. which can be used to treat estrogenic deficiency, and prevent osteoporosis and cardiovascular diseases in **menopause** women. The invention further relates to a method for the prodn. of said estro-gestagenic compns.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:495495 CAPLUS
DOCUMENT NUMBER: 137:195772
TITLE: Progestin effects on human endometrium in vitro
AUTHOR(S): Charpin, Colette; Illouz, Severine; Dales, Jean-Philippe; Lavaut, Marie-Noelle; Allasia, Claude; Boubli, Leon
CORPORATE SOURCE: Laboratoire d'Anatomie Pathologique, Faculte de Medecine Nord, Marseille, 13916, Fr.
SOURCE: Bulletin de l'Academie Nationale de Medecine (Paris, France) (2002), 186(1), 125-146
CODEN: BANMAC; ISSN: 0001-4079
PUBLISHER: Academie Nationale de Medecine
DOCUMENT TYPE: Journal
LANGUAGE: French
IT **58652-20-3**, Nomegestrol acetate
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(progestin effects on human endometrium in vitro)
RN 58652-20-3 CAPLUS
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB In order to obtain a better evaluation of the epithelial proliferation of the human endometrium, we developed an "in vitro" model to quantify the effects of hormonal treatments, as an "hormonogram". We particularly aimed to evaluate the effects of steroids used in the replacement hormone therapy during **menopause** in the view of predicting and preventing the development of precancerous lesions of the endometrium. This study has evaluated the effects of different progestins currently used in hormone therapy, progesterone, medroxy-progesterone acetate (MPA), nomegestrol acetate (TX), norethindrone acetate (NOR) on human proliferative endometrium explant culture, using two means: prostaglandin F2.alpha. (PGF2.alpha.) output in medium culture, and immunoexpression of estradiol receptor (ER), progesterone receptor (PR) and proliferative antigen Ki67 in tissue. After culture, quant. studies on ER or PR immunoexpression could be assessed by image anal. procedure in contrast to Ki67 immunoexpression too weak low in non tumorous endometrium to be quantified. PGF2.alpha. output, was decreased by progesterone, TX and MPA in both proliferative endometrium subtypes. With regards to receptor immunoexpression, progesterone only decreased PR expression in proliferative endometrium. PR immunoexpression in stromal cells was decreased by all progestins in homogeneous proliferative endometrium explants. TX decreased PR and ER expression in glands and stroma of homogeneous proliferative endometrium. MPA exhibited similar effects but only on heterogeneous proliferative endometrium. In brief, our results show that in vitro progestative treatment on endometrium reduced PGF2.alpha. output and decreased PR and/or ER immunoexpression, although the in vitro effects of each progestin were not similar and varied with the endometrium subtype (proliferative homogeneous or heterogeneous). This study opens new fields of research particularly to investigate the endometrial proliferative activity using explant culture.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:220377 CAPLUS
DOCUMENT NUMBER: 136:252498
TITLE: Novel topical oestroprogestational compositions with systemic effect
INVENTOR(S): Gray, Georges; Villet, Bertrand; Paris, Jacques; Thomas, Jean-Louis
PATENT ASSIGNEE(S): Laboratoire Theramex Sam, Monaco
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022132	A2	20020321	WO 2001-FR2865	20010914
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
FR 2814074	A1	20020322	FR 2000-11791	20000915
AU 2001090026	A5	20020326	AU 2001-90026	20010914
BR 2001007216	A	20020709	BR 2001-7216	20010914
EP 1265617	A2	20021218	EP 2001-969895	20010914
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NO 2002002292	A	20020715	NO 2002-2292	20020514

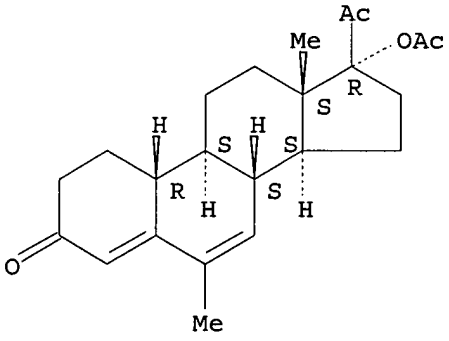
PRIORITY APPLN. INFO.: FR 2000-11791 A 20000915
WO 2001-FR2865 W 20010914

IT **58652-20-3**, Nomegestrol acetate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel topical oestroprogestational compns. with systemic effect)

RN 58652-20-3 CAPLUS

CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

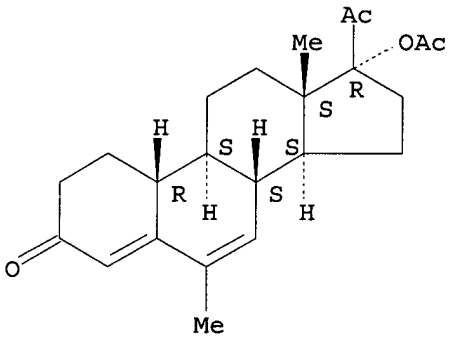


AB The invention concerns the field of therapeutic chem. and more particularly the prodn. of novel galenic forms to be applied on the skin. More particularly, it concerns a topical hormonal compn. with systemic effect for hormonal treatment of perimenopause and **menopause** as well as for treating ovarian hormonal deficiency in a woman suffering from amenorrhea. The invention is characterized in that it comprises, as active principles, a progestational deriv. of the 19-norprogesterone and estradiol or one of its derivs., a carrier for systemic delivery of said active principles, selected among the group consisting of a film-forming agent, a gelling agent and mixts. thereof, combined with a mixt. of excipients suited for producing a gelled and/or film-forming pharmaceutical form. A topical gel contained nomegestrol acetate 0.4, estradiol 0.1, Carbopol-1342 0.5, propylene glycol 6, transcutol 5, EDTA

0.05, triethanolamine 0.3, water 42.65, and ethanol 45%. Effectiveness of the compn. was tested in female volunteers.

L19 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:856712 CAPLUS
DOCUMENT NUMBER: 136:178101
TITLE: Effects of different types of hormone replacement therapy on mammographic density
AUTHOR(S): Colacurci, Nicola; Fornaro, Felice; De Franciscis, Pasquale; Palermo, Mario; del Vecchio, Walter
CORPORATE SOURCE: Outpatient Menopausal Clinic, Institute of Gynaecology and Obstetrics, School of Medicine, Second University of Naples, Naples, 80134, Italy
SOURCE: Maturitas (2001), 40(2), 159-164
CODEN: MATUDK; ISSN: 0378-5122
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **58652-20-3**, Nomegestrol acetate
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of different types of hormone replacement therapy on mammog. d.)
RN 58652-20-3 CAPLUS
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



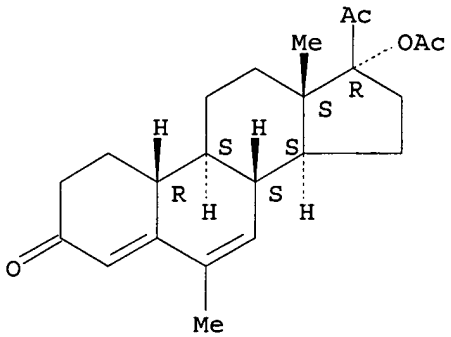
AB Objectives: to evaluate the effects of different types of hormone replacement therapy (HRT) on mammog. d. in postmenopausal women. Methods: In a prospective 1-yr study, 121 healthy postmenopausal women were allocated to one of the following five study groups: twenty-six women were treated with continuous transdermal 17beta-estradiol 50 mcg/die plus acetate nomegestrol 5 mg/die sequentially added for 12 days per mo (Group A); 25 women were treated with continuous transdermal 17beta-estradiol 50 mcg/die plus acetate nomegestrol 2.5 mg/die added every day (Group B); 23 women were treated with continuous transdermal 17beta-estradiol 50 mcg/die (Group C); 24 women were treated with tibolone 2.5 mg/die (Group D); and 23 women not receiving any medication represented the control group (Group E). At the time of recruitment and after 12 mo a two-view mammog. was performed to evaluate mammog. d. according to a quant. method: type 1 (less than 25% of mammary gland covered by dense tissue), type 2 (from 25 to 75% of total glandular area covered by dense tissue), type 3 (more than 75% of mammary parenchyma covered by dense tissue). Results: After 12 mo

of HRT, seven out of 20 patients (35%) in group A, nine of 21 patients (42.85%) in group B, four out of 19 patients (21%) in group C and two of 20 patients (10%) in group D, showed an increase in mammog. d. No variation of d. was obsd. at the second mammog. test in the control group. The mammog. d. increase which occurred in groups A, B and C was statistically significant ($P<0.05$) when compared with group E; no statistically significant difference ($P=0.49$) was found in mammog. d. increase between group D and group E. When the different treatment types were compared each other, a statistically significant difference ($P=0.04$) was found only between the mammog. d. increase occurring in groups B and D. Conclusions: HRT may cause an increase of mammog. d. The frequency of the d. increase is related to the type of HRT and a replacement therapy including a progestin, esp. in continuous combination with estrogen, leads to more evident mammog. changes. Tibolone does not significantly affect mammog. d.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:566988 CAPLUS
DOCUMENT NUMBER: 135:327515
TITLE: Withdrawal of hormone replacement therapy is associated with significant vertebral bone loss in postmenopausal women
AUTHOR(S): Tremollieres, F. A.; Pouilles, J.-M.; Ribot, C.
CORPORATE SOURCE: Menopause and Bone Metabolic Disease Unit, CHU Rangueil, Toulouse, F-31403, Fr.
SOURCE: Osteoporosis International (2001), 12(5), 385-390
CODEN: OSINEP; ISSN: 0937-941X
PUBLISHER: Springer-Verlag London Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **58652-20-3**, Nomegestrol acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(withdrawal of hormone replacement therapy is assocd. with significant vertebral bone loss in postmenopausal women)
RN 58652-20-3 CAPLUS
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB This study aimed to assess the changes in vertebral bone mineral d. (BMD)

after cessation of hormone replacement therapy (HRT) in postmenopausal women who had been treated on a long-term basis. Fifty healthy postmenopausal women who had been followed both during the course of HRT and after cessation of treatment in our **menopause** clinic were included in this study. All women had started HRT within the first 3 yr after the postmenopause and had received HRT (either 1.5 mg/day of 17.beta.-estradiol given percutaneously or 50 .mu.g/day of 17.beta.-estradiol given as a transdermal patch, combined in all women with natural progesterone or a 19-norprogesterone deriv.) for a mean 5.+-.2.4 yr. In all women, vertebral BMD was assessed during the course of HRT up to the last 6 mo before estrogen withdrawal, then at least once within the first 18 mo after cessation of treatment. Of the initial population, 30 women were addnl. reviewed later on and up to 8 yr after cessation of treatment (mean duration of follow-up for the whole population: 3.9.+-.1.7 yr). Rates of changes in vertebral BMD were compared with those detd. in a group of healthy untreated women who had been followed within the first years of postmenopause during the same time period as the study population. In the study group, bone loss was found to accelerate within the first 2 yr after HRT withdrawal and the annual rate of loss was identical to that which occurs within the first 2 yr of post-**menopause** in untreated women (-1.64% .+-. 1.3% vs. -1.52.+-.0.9%, NS). Beyond this first 2-yr time period, the annual rate of bone loss decreased as a function of time following cessation of treatment, as was obsd. following the **menopause** in untreated women (between 3 and 5 yr: -0.83% + 1.35% in the study group vs. -0.70% .+-. 0.8% in the control group, NS). On av., 3 yr after cessation of HRT mean vertebral BMD when expressed as a Z-score was significantly higher (-0.13 vs. -0.89, $p<0.01$) than at baseline, before HRT was started, which suggested a lasting beneficial effect on bone mass. However, even though our findings do not support the hypothesis that bone loss might continue to be accelerated several years after cessation of treatment we cannot fully address the question as to whether any residual benefit on bone mass over a longer period of time may be obsd. In conclusion, the pattern of bone loss obsd. after cessation of estrogen therapy was found to be comparable to that which occurs in younger women within the first years after the **menopause**. Such a pattern needs to be kept in mind when the decision to stop HRT is taken, esp. in women who were given HRT to prevent osteoporosis. The issue of assessing their risk of fracture several years after cessation of treatment thus needs to be addressed.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

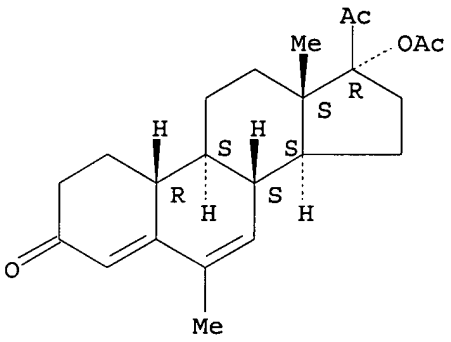
L19 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:319731 CAPLUS
DOCUMENT NUMBER: 134:316160
TITLE: Hormonal composition based on a progestational agent and an estrogen
INVENTOR(S): Paris, Jacques; Thomas, Jean-Louis
PATENT ASSIGNEE(S): Laboratoire Theramex, Monaco
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001030356	A1	20010503	WO 1999-FR2588	19991025

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
WO 2001030357 A1 20010503 WO 2000-FR2939 20001024
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1227814 A1 20020807 EP 2000-971476 20001024
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL
NO 2002001949 A 20020425 NO 2002-1949 20020425
PRIORITY APPLN. INFO.: WO 1999-FR2588 W 19991025
WO 2000-FR2939 W 20001024

IT **58652-20-3**, Nomegestrol acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hormonal compn. based on progestational agent and estrogen)
RN 58652-20-3 CAPLUS
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



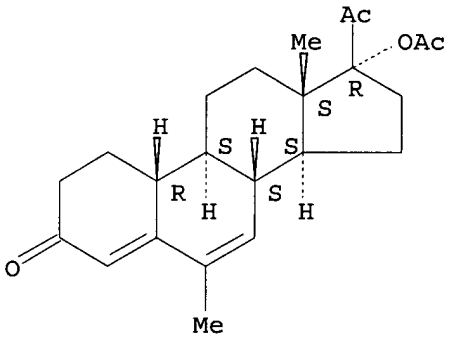
AB The invention concerns the field of therapeutic chem. and more particularly the field of hormonal pharmaceutics technique. More precisely, it concerns novel hormonal compns. formed by an progestogen-estrogen combination consisting of an estrogen compd. and a progestational compd., assocd. or mixed with one or several pharmaceutically acceptable inert non-toxic carriers designed for oral administration. The invention also concerns the use of the progestogen-estrogen mixt. wherein the estrogen constituent and the progestogen constituent are administered in combination. The combined assocn. can be prescribed continuously or intermittently, so as to produce a compn. for treating estrogen deficiencies, preventing osteoporosis and cardiovascular diseases in postmenopausal women. The invention further concerns a method for prepg. said novel pharmaceutical progestogen-estrogen compns. A tablet contained estradiol 0.811, nomegestrol acetate 0.338, lactose 71.238, cellulose 15.032, povidone 7.297, Precirol AT05 1.503, colloidal silica 0.540, and crospovidone

3.243%. Antimitotic effects of the compn. in endometrial cells was studied.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:854101 CAPLUS
DOCUMENT NUMBER: 134:37255
TITLE: Nomegestrol acetate and vascular reactivity: nonhuman primate experiments
AUTHOR(S): Paris, J. M.; Williams, K. J.; Hermsmeyer, K. R.; Delansorne, R.
CORPORATE SOURCE: BP 59, Laboratoire Theramex, 98007, Monaco
SOURCE: Steroids (2000), 65(10-11), 621-627
CODEN: STEDAM; ISSN: 0039-128X
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **58652-20-3**, Nomegestrol acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(nomegestrol acetate and vascular reactivity in nonhuman primates in relation to role of progestins in hormone replacement therapy)
RN 58652-20-3 CAPLUS
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



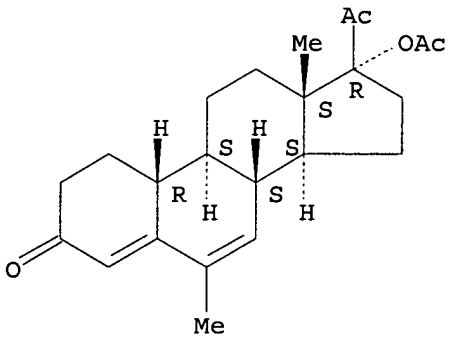
AB Prevention of coronary artery disease has been recognized as a major benefit of estrogen replacement therapy (ERT) in postmenopausal women. However, endometrial hyperplasia induced by unopposed ERT has raised important safety concerns. Progesterone or synthetic progestins have been used in combined hormone replacement therapy (HRT) to prevent endometrial cancer risk. Therefore, a major concern has been to ensure that the vascular beneficial effects of estrogens are not opposed when combined with progestins. Nomegestrol acetate (NOMAC) is an orally active progestin widely prescribed for HRT. Its vascular effects were evaluated in two models of coronary vascular reactivity in primates: the paradoxical vasoconstriction to acetylcholine (Ach) coronary infusion after 5 mo of mildly atherogenic diet in ovariectomized (OVX) Cynomolgus monkeys and the pharmacol. evoked coronary vasospasm in the OVX Rhesus monkey. In the first model, after 3 mo of continuous oral administration in the diet at 0.1 mg/kg/day, E2 prevented the paradoxical response to Ach, alone as well as combined with 0.25 mg/kg/day NOMAC, whereas NOMAC counteracted the

endometrial stimulation. In the second model, after one artificial cycle consisting of 28 days of E2 s.c. implant and of daily oral gavage with 1 mg/kg/day of NOMAC for the last 14 days, no vasospasm (0 of 11 tested animals) occurred when the complete challenge protocol, including serotonin and the thromboxane agonist U46619, was administered to OVX Rhesus monkeys. In the balanced crossover design, identical artificial cycles with medroxyprogesterone acetate (MPA) at the same dose resulted in 7 vasospasms in 12 animals. In parallel, effective progestative activity was demonstrated by a secretory pattern in endometrial sections obtained at the end of the cycle. In these two nonhuman primate cardiovascular models, NOMAC did not have the negating effects obsd. with MPA.

REFERENCE COUNT: 93 THERE ARE 93 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:538390 CAPLUS
DOCUMENT NUMBER: 133:291258
TITLE: Effects of hormone replacement therapy on postmenopausal uterine myoma
AUTHOR(S): Colacurci, Nicola; De Franciscis, Pasquale; Cobellis, Luigi; Nazzaro, Giovanni; De Placido, Giuseppe
CORPORATE SOURCE: Outpatient Menopausal Clinic, Second University of Naples, Naples, 80134, Italy
SOURCE: Maturitas (2000), 35(2), 167-173
CODEN: MATUDK; ISSN: 0378-5122
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **58652-20-3**, Nomegestrol acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of hormone replacement therapy on postmenopausal uterine myoma)
RN 58652-20-3 CAPLUS
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB The effects of sequential continuous hormone replacement therapy (HRT) on myoma size and on pulsatility index (PI) of uterine arteries were evaluated and the correlation between uterine artery flow impedance and the growth rate of myoma in women receiving HRT was verified. In a prospective 1-yr study 60 postmenopausal women were enrolled into three

study-groups to receive continuous transdermal 17.beta.-estradiol 0.05 mg/day plus nomegestrol acetate 5 mg/day sequentially added: 20 patients (group A) unaffected by uterine myomas, 20 patients (group B) with single asymptomatic myoma < 3 cm/14 cm3, 20 patients (group C) with single asymptomatic myoma > 3 cm/14 cm3. The changes in myoma vol. and in PI were assessed by means of transvaginal ultrasonog. scan every 3 mo. The patients with myoma were divided into two subgroups: quiescent myoma (B1, C1) and growing myoma (B2, C2). Results: No significant increase of uterine fibroids vol. was found after 1-yr HRT (24.14 .+-. 20.02 .fwdarw. 28.81 .+-. 30.02 cm3). Six out of eight myomas growing during HRT belonged to group C. The uterine artery basal PI value of group A was significantly higher (P < 0.01) than the corresponding PI in group B and C. At 3 mo follow-up, uterine artery PI was significantly higher (P < 0.01) than the basal value in both group B (1.70 .+-. 0.22 .fwdarw. 1.88 .+-. 0.16) and C (1.59 .+-. 0.28 .fwdarw. 1.92 .+-. 0.21). The baseline PI values in group B1 and C1 were significantly higher than the baseline values obsd. in group B2 and C2 (1.76 .+-. 0.17 vs. 1.32 .+-. 0.02, 1.76 .+-. 0.16 vs. 1.24 .+-. 0.08) and significantly lower than those obsd. in group A (2.39 .+-. 0.47). After 3 mo of HRT, the PI values were not significantly higher than the baseline values in groups B1 and C2 (1.76 .+-. 0.17 .fwdarw. 1.90 .+-. 0.17; 1.24 .+-. 0.08 .fwdarw. 1.74 .+-. 0.16), while they were significantly higher in group C1 (1.76 .+-. 0.16 .fwdarw. 2.01 .+-. 0.17). Conclusions: Sequential continuous HRT does not increase the vol. of the uterine myoma. The findings of very low resistance index in the uterine arteries of women with growing myoma may indicate the risk of growth of the neoplasia during HRT. The assessment of PI in the uterine arteries could be helpful in predicting the growth rate of the myomas before starting HRT.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

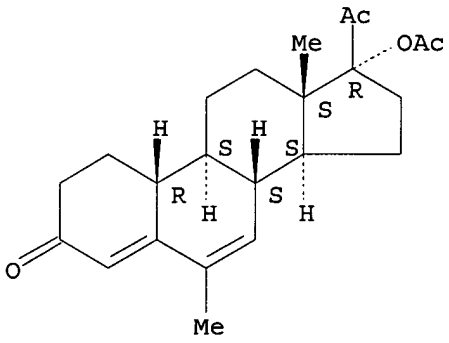
L19 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:626026 CAPLUS
DOCUMENT NUMBER: 131:262597
TITLE: Topical hormonal composition with systemic effects for the treatment of progesterone deficiency
INVENTOR(S): Lanquetin, Michel; Paris, Jacques; Thomas, Jean-Louis
PATENT ASSIGNEE(S): Laboratoire Theramex, Monaco
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9948477	A1	19990930	WO 1999-FR680	19990323
W: AU, BR, CA, CN, CU, CZ, HU, ID, IL, IN, JP, KR, MX, NO, NZ, PL, RU, SG, TR, US, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2776191	A1	19990924	FR 1998-3533	19980323
FR 2776191	B1	20020531		
CA 2324904	AA	19990930	CA 1999-2324904	19990323
AU 9928451	A1	19991018	AU 1999-28451	19990323
EP 1066030	A1	20010110	EP 1999-909078	19990323
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

	IE, FI				
BR 9909027	A	20011211	BR 1999-9027		19990323
JP 2002507561	T2	20020312	JP 2000-537527		19990323
NO 2000004745	A	20001120	NO 2000-4745		20000922
PRIORITY APPLN. INFO.:			FR 1998-3533	A	19980323
			WO 1999-FR680	W	19990323

IT **58652-20-3**, Nomegestrol acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(topical hormonal compn. with systemic effects for treatment of progesterone deficiency)
RN 58652-20-3 CAPLUS
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB A topical hormonal compn. with systemic effect to remedy progesterone deficiency in the pre-menopausal woman and as hormonal substitute for the post-menopausal woman is disclosed. The compn. comprises, as active principle, a gestagenic derived from 19-nor progesterone, a carrier for systemic passage of said active principle selected from the group consisting of a solubilizing agent, an agent promoting absorption, a film-forming agent, a gelling agent or their mixts., assocd. or mixed with appropriate carriers for producing a gelled and/or film-forming pharmaceutical form. A topical gel contained nomegestrol acetate 0.4, propylene glycol 6.00, Transcutol 5.00, Carbopol-1342 0.5, EDTA 0.05, triethanolamine 0.30, water 42.75, and ethanol 45.00%.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:790272 CAPLUS
DOCUMENT NUMBER: 130:177698
TITLE: Continuous hormone replacement therapy for **menopause** combining nomegestrol acetate and gel, patch, or oral estrogen: A comparison of amenorrhea rates
AUTHOR(S): Blanc, Bernard; Cravello, Ludovic; Micheletti, Marie-Christine; d'Ercole, Claude; Zartarian, Marie
CORPORATE SOURCE: Service de Gynecologie Obstetrique B, Hopital de la Conception, Marseille, Fr.
SOURCE: Clinical Therapeutics (1998), 20(5), 901-912
CODEN: CLTHDG; ISSN: 0149-2918

09284147

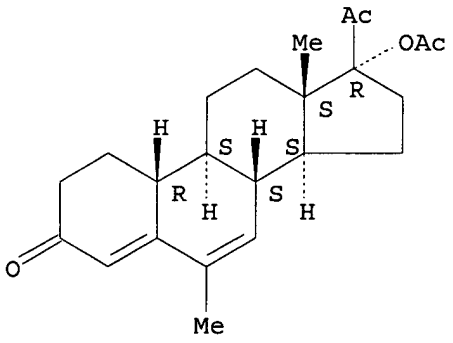
PUBLISHER: Excerpta Medica
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **58652-20-3**, Nomegestrol acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amenorrhea rates in continuous hormone replacement therapy combining nomegestrol acetate and gel, patch, or oral estrogen in **menopause** in women)

RN 58652-20-3 CAPLUS

CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB This open-label, prospective, randomized, multicenter trial compared the incidence of amenorrhea in 54 postmenopausal women (mean age, 54.9 yr) who underwent six 4-wk cycles of continuous hormone replacement therapy combining a progestin-nomegestrol acetate 2.5 mg/d-plus one of three estrogens: percutaneous 17.beta.-estradiol gel (1.5 mg/d, group A), transdermal 17.beta.-estradiol patch (50 .mu.g/d, group B), or oral estradiol valerate (2 mg/d, group C). Based on an intent-to-treat anal., the rate of amenorrhea varied significantly according to which estrogen prepn. was used. Calcd. cycle by cycle, rates of amenorrhea were 67% to 83% for group A, 25% to 56% for group B, and 53% to 61% for group C. Overall rates of persistent amenorrhea were not statistically different between groups for cycles 1 through 3, but for cycles 4 through 6, significantly more women in groups A and C (67% and 46%, resp.) experienced amenorrhea than did those in group B (12%). Amenorrhea rates for the entire six-cycle period were 78% for group A, 48% for group B, and 60% for group C. These differences were not statistically significant. The differences in rates could not be attributed to endometrial atrophy, since when measured by transvaginal sonog., endometrial thickness did not differ significantly between groups. Of the original population, 7% withdrew prematurely because of bleeding. The data for all three groups confirmed that in two out of three women, the occurrence of amenorrhea during the first three cycles predicted continuation of amenorrhea during subsequent cycles and that for 51% of women, .ltoreq.10 days of bleeding during the first three cycles predicted amenorrhea during the last three cycles. Calcd. as a function of the no. of women included in the trial, the percentage of amenorrheic women (evaluated cycle by cycle or for the second three-cycle period) was highest when the progestin was combined with percutaneous 17.beta.-estradiol gel, although findings were similar with estradiol valerate. The percutaneous 17.beta.-estradiol gel was also

assocd. with a higher percentage of amenorrheal cycles than was estradiol valerate or transdermal estrogen, although differences were significant only in comparison with the transdermal formulation. This difference may have pos. clin. implications.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE 'REGISTRY' ENTERED AT 15:30:52 ON 09 JAN 2003
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L2 1 S NOMEGESTROL ACETATE

FILE 'REGISTRY' ENTERED AT 15:32:41 ON 09 JAN 2003
L3 0 S L1
L4 1 S L2

FILE 'CAPLUS' ENTERED AT 15:34:27 ON 09 JAN 2003
L5 78 S L4
L6 78 S L2
L7 22 S L6 AND ESTROGEN
L8 9 S L7 AND TREATMENT
L9 1 S L7 AND POST MENOPAUSE
L10 5 S L7 AND CARDIOVASCULAR
L11 2 S L7 AND BLEEDING
L12 30 S L5 AND ESTRADIOL
L13 1 S L12 AND POST MENOPAUSE
L14 0 S L12 AND HARMONE REPLACEMENT
L15 3 S ESTROGENIC DEFICIENCIES
L16 30 S L5 AND ESTRADIOL
L17 32 S L5 AND WOMEN
L18 7 S L17 AND CONTRACEPTION
L19 17 S L5 AND MENOPAUSE
L20 11 S L19 AND ESTROGEN

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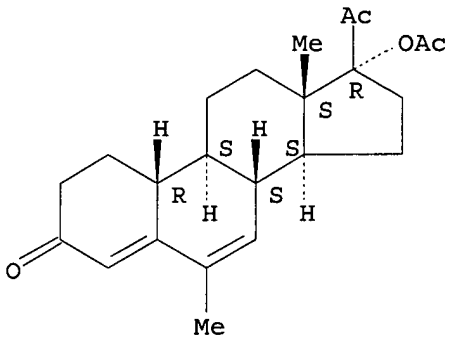
L19 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:188983 CAPLUS
DOCUMENT NUMBER: 128:266398
TITLE: Neuroendocrine effects of different estradiol-progestin regimens in postmenopausal women
AUTHOR(S): Stomati, M.; Bersi, C.; Rubino, S.; Palumbo, M.; Comitini, G.; Genazzani, A. D.; Santre, M.; Petraglia, F.; Genazzani, A. R.
CORPORATE SOURCE: Department of Obstetrics and Gynecology, University of Pisa, Pisa, Italy
SOURCE: Maturitas (1997), 28(2), 127-135
CODEN: MATUDK; ISSN: 0378-5122
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **58652-20-3**, Nomegestrol acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(neuroendocrine effects of estradiol-progestin regimens in postmenopausal women)

RN 58652-20-3 CAPLUS

CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB New regimens and routes of administration of hormonal replacement therapy (HRT) in climateric women are becoming available. Since there is no information on the neuroendocrine effects of sequential combined treatment with 17.beta.-estradiol and a progestin, the present study evaluated the neuroendocrine, clin. vasomotor and psychol. changes before and after different sequential combined HRT regimens (17.beta.-estradiol plus nomegestrol acetate, or cyproterone acetate, or vaginal progesterone). Vasomotor and behavioral effects were evaluated by using the Kupperman score, while changes in plasma endorphin (.beta.-END) levels were used as marker of neuroendocrine effects. Postmenopausal women were randomly divided into three groups; all women received continuous 17.beta.-estradiol (50 mg, transdermal) and each group was sequentially treated with different progestins for 12 days/mo: group A, cyproterone acetate (5 mg, p.o.); group B, nomegestrol acetate (5 mg, p.o.); and group C, progesterone (100 mg, vaginal cream). A group of healthy fertile women served as control. Before and after 6 mo of HRT, postmenopausal women underwent an evaluation of subjective Kupperman score and two neuroendocrine tests: (a) naloxone (4 mg, i.v.) and (b) clonidine (1.25 mg, i.v.). Plasma .beta.-END levels were measured before and at 15, 30, 45, 60 and 90 min after drug injection. Control women were studied by administering the two neuroendocrine tests only once. Postmenopausal women before HRT showed a pathol. Kupperman and no changes of plasma .beta.-END levels in response to the clonidine and naloxone tests score. On the contrary the increase was significant in healthy women. In each of the three groups of treated women both naloxone and clonidine tests induced a significant increase in plasma .beta.-END levels. After 6 mo of HRT, an improvement of vasomotor and psychol. symptoms was shown by a decrease of Kupperman score. The present study indicates that sequential treatment with transdermal 17.beta.-estradiol and progestin, no matter which progestin was used, restores the .beta.-END release, and improves vasomotor and psychol. symptoms.

L19 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:226799 CAPLUS

DOCUMENT NUMBER: 126:216684

TITLE: Novel hormonal medicaments and use thereof for correcting estrogen deficiencies

09284147

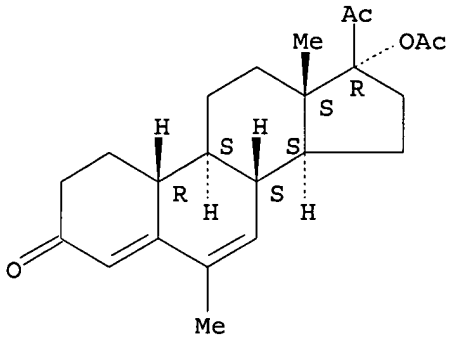
INVENTOR(S): Lanquetin, Michel; Paris, Jacques; Thomas, Jean-Louis
PATENT ASSIGNEE(S): Laboratoire Theramex, Monaco; Lanquetin, Michel; Paris, Jacques; Thomas, Jean-Louis
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9704784	A1	19970213	WO 1996-IB754	19960729
W: AU, BR, CA, CN, CZ, FI, HU, IL, JP, KR, MX, NO, RU, SG, US, VN				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2737411	A1	19970207	FR 1995-9364	19950801
FR 2737411	B1	19971017		
CA 2201368	AA	19970213	CA 1996-2201368	19960729
AU 9663674	A1	19970226	AU 1996-63674	19960729
AU 722355	B2	20000727		
EP 783310	A1	19970716	EP 1996-923018	19960729
EP 783310	B1	20021009		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1167438	A	19971210	CN 1996-191100	19960729
BR 9606549	A	19980623	BR 1996-6549	19960729
JP 10507207	T2	19980714	JP 1996-507406	19960729
CZ 289706	B6	20020313	CZ 1997-967	19960729
RU 2188641	C2	20020910	RU 1997-108279	19960729
AT 225659	E	20021015	AT 1996-923018	19960729
ZA 9606545	A	19970508	ZA 1996-6545	19960801
TW 473390	B	20020121	TW 1996-85111673	19960924
NO 9701449	A	19970530	NO 1997-1449	19970326
US 5891867	A	19990406	US 1997-817329	19970424

PRIORITY APPLN. INFO.: FR 1995-9364 A 19950801
WO 1996-IB754 W 19960729

IT **58652-20-3**, Nomegestrol acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel hormonal medicaments for correcting estrogen deficiencies)
RN 58652-20-3 CAPLUS
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

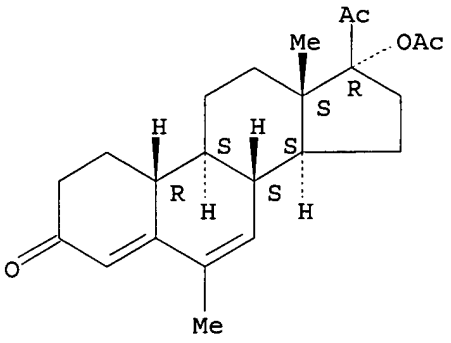
Absolute stereochemistry.



AB A trisequential, oestroprogestogen hormonal combination characterized in that it comprises unit doses contg. only one estrogen, unit doses contg. a combination of one estrogen and one progestogen, and unit doses contg. only one carrier. The trisequential delivery mode aims at compensating functional disorders caused by menopausal or pre-menopausal hypoestrogenism. Formulation of 1.5 mg 17.beta.-estradiol tablets and 2.5 mg nomegestrol acetate tablets are disclosed. The efficacy of tablets in treatment of hot flashes in menopausal women are reported.

L19 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:746706 CAPLUS
DOCUMENT NUMBER: 126:42825
TITLE: The antigonadotropic activity of progestins (19-nortestosterone and 19-norprogesterone derivatives) is not mediated through the androgen receptor
AUTHOR(S): Couzinet, Beatrice; Young, Jacques; Brailly, Sylvie; Chanson, Philippe; Thomas, Jean Louis; Schaison, Gilbert
CORPORATE SOURCE: Service Endocrinologie Maladies Reproduction, Hop. Bicetre, Kremlin, 94275, Fr.
SOURCE: Journal of Clinical Endocrinology and Metabolism (1996), 81(12), 4218-4223
CODEN: JCEMAZ; ISSN: 0021-972X
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **58652-20-3**, Nomegestrol acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antigonadotropic activity of progestins is not mediated by androgen receptor)
RN 58652-20-3 CAPLUS
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



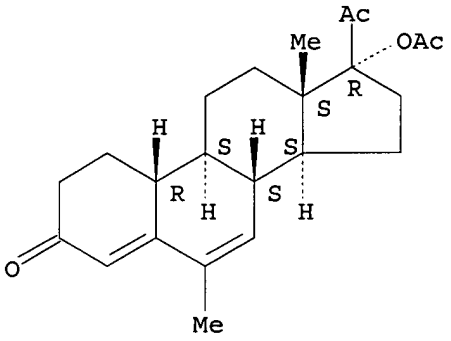
AB To further study the mechanism of the antigonadotropic activity of progestins, the effects of a 19-nortestosterone deriv., norethisterone acetate (NETA), and a 19-norprogesterone deriv., nomegestrol acetate (NOMA), were compared. The aim was to assess whether their action is exerted via the androgen receptor. Ten healthy postmenopausal women were treated for five monthly periods of 24 days sepd. by 10 days in a randomized crossover design. Transdermal estradiol, Estraderm TTS (25 .mu.g; one patch every 3 days), was given from days 1-24 during the five periods. On the last 12 days, of each estradiol treatment, they all received a placebo, NOMA (5 mg/day), NOMA in assocn. with the nonsteroidal antiandrogen, flutamide (FLU; 250 mg, twice a day), NETA (10 mg/day), or NETA plus FLU. On the other hand, three castrated patients with complete androgen insensitivity (CAI) received NOMA and NETA for two periods of 12 days sepd. by 3 wk. In postmenopausal women, the effects of NOMA and NETA on metabolic parameters were studied. Only NETA decreased high d. lipoprotein cholesterol. Plasma LH, FSH, and estradiol were measured during each treatment period. A significant decrease in mean plasma LH and FSH levels and their responses to exogenous GnRH was obsd. with NOMA and NETA treatments compared to placebo. The pulsatile frequency, but not the amplitude, of LH was significantly decreased during both treatments. Interestingly, the effects of both progestins on gonadotropins were not antagonized by FLU administration. In the patients with CAI, the pulsatile study of gonadotropins was performed before and on day 12 of NOMA and NETA treatments. As in postmenopausal women, both progestins induced similar decreases in LH and FSH. In conclusion, a 19-nortestosterone deriv., NETA, and a 19-norprogesterone deriv., NOMA, have similar antigonadotropic activities. This effect, not antagonized by FLU and obsd. in patients with CAI, is not mediated via the androgen receptor. The absence of deleterious effects of 19-norprogesterone derivs. on metabolic parameters should favor the therapeutic use of these compds.

L19 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1987:149754 CAPLUS
DOCUMENT NUMBER: 106:149754
TITLE: Effects of progesterone and nomegestrol acetate on rabbit endometrial epithelium. Scanning-electron-microscopic study
AUTHOR(S): Paris, J. M.; Mrena, E.; Lanquetin, A.; Marchal, G. M.; Thevenot, R.
CORPORATE SOURCE: Lab. Theramex, Monaco, 98000, Monaco
SOURCE: Journal de Pharmacologie (1986), 17(4), 508-14
CODEN: JNPHAG; ISSN: 0021-793X
DOCUMENT TYPE: Journal
LANGUAGE: French

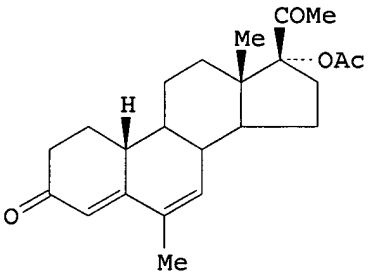
09284147

IT **58652-20-3**, Nomegestrol acetate
RL: BIOL (Biological study)
(uterus endometrium morphol. response to estradiol and, progesterone in comparison with)
RN 58652-20-3 CAPLUS
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



I

AB Priming of immature rabbits with estradiol [50-28-2] followed by injection of progesterone [57-83-0] (2-12.5 mg) s.c. for 5 days resulted in changes in endometrial morphol. as detected by SEM which were similar to the changes occurring in postmenopausal women on estroprogestative therapy. Similar changes were obsd. when nomegestrol acetate (I) [**58652-20-3**] (0.25-12.5 mg, orally) was substituted for progesterone. Thus, the 19-norprogesterone deriv. displayed similar activity to the parent compd.

L19 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1986:102648 CAPLUS
DOCUMENT NUMBER: 104:102648
TITLE: Study on the pharmacokinetics of a progestative drug using a carbon-14-labeled product or a cold method
AUTHOR(S): Viot, G.; Thevenot, R.; Paris, J.; Milano, G.; Hopkins, R.
CORPORATE SOURCE: Lab. Theramex, Monaco, 98007, Monaco

09284147

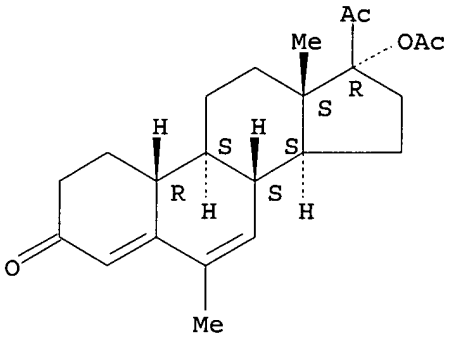
SOURCE: Journal de Pharmacie Clinique (1985), 4(Hors Ser. 1), 127-36
CODEN: JPCLDE; ISSN: 0291-1981
DOCUMENT TYPE: Journal
LANGUAGE: French

IT **58652-20-3**
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(pharmacokinetics of, in humans and lab. animal and monkey)

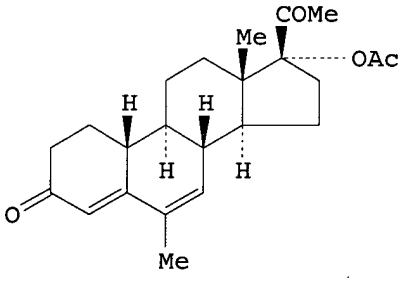
RN 58652-20-3 CAPLUS

CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



I

AB The pharmacokinetics of TX 066 (nomegestrol acetate) (I) [**58652-20-3**] were detd. in rats, cynomolgus monkeys, and menopausal women. Both 14C-labeled and cold I (urinary and blood anal. by HPLC) were used. Regardless of the species, absorption of I was rapid, with peak plasma levels obsd. at 2 h in female monkeys. Distribution was also rapid, with radioactivity appearing in rat liver and digestive tract. No abnormal accumulation of I was found, esp. in fat. The kinetics of I in plasma were similar for both radiolabeled and cold I. On repeated administration of 5 mg I/day for 10 days, plasma steady state levels were obtained in 4-5 days. Individual I kinetics were qual. similar on the 1st and 10th days. Excretion was via the urine and feces with no radioactivity found in expired CO2. Urinary excretory products were

mainly sulfate and glucuronide metabolites. Low levels of unchanged I were found in the stool, indicating high absorption. Thus, I pharmacokinetics were characterized by a rapid absorption, high metab., and slow excretion.

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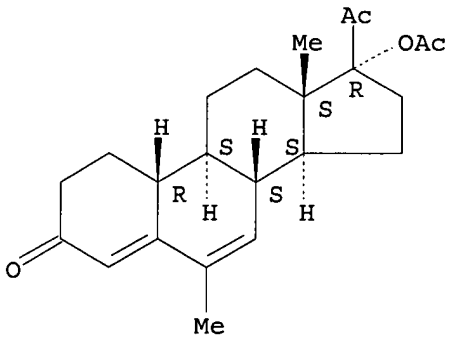
L20 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:859068 CAPLUS
DOCUMENT NUMBER: 137:362854
TITLE: Simvastatin, transdermal patch, and oral **estrogen**-progestogen preparation in early-postmenopausal hypercholesterolemic women: a randomized, placebo-controlled clinical trial
AUTHOR(S): Vigna, Giovanni B.; Donega, Paola; Zanca, Rosanna; Barban, Angela; Passaro, Angelina; Pansini, Francesco; Bonaccorsi, Gloria; Mollica, Gioacchino; Fellin, Renato
CORPORATE SOURCE: Department of Clinical and Experimental Medicine, Section of Internal Medicine II, University of Ferrara, Ferrara, 44100, Italy
SOURCE: Metabolism, Clinical and Experimental (2002), 51(11), 1463-1470
CODEN: METAAJ; ISSN: 0026-0495
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **58652-20-3**, Nomegestrol acetate
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(simvastatin transdermal patch and oral **estrogen**-progestogen prepn. in early-postmenopausal hypercholesterolemic women)
RN 58652-20-3 CAPLUS
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Hormone replacement therapy (HRT) seems to have a favorable influence on the plasma lipid profile. Only a few investigations have examd. the effects of HRT vs. hepatic hydroxymethyl glutaryl CoA (HMG-CoA) reductase inhibitors. We compared the relative effects of different hypolipidemic strategies on lipoproteins and coagulative parameters in women with recent-onset spontaneous **menopause**. In this 24-wk,

placebo-controlled trial, 60 consecutive healthy women aged .gtoreq. 45 yr, with amenorrhea from 6 to 60 mo (mean, 1.9.+-.1.4 yr), serum FSH greater than 40 U/L, and slight to moderate hypercholesterolemia (low-d. lipoprotein-cholesterol [LDL-C] 160 to 250 mg/dL, high-d. lipoprotein-cholesterol [HDL-C] < 75 mg/dL, and triglycerides < 200 mg/dL) were enrolled and randomized to dietetic advice (placebo group), simvastatin 10 mg, 0.625 mg of conjugated equine **estrogen** (CEE), or 50 .mu.g **estrogen** transdermal patch (ETP). In the latter 2 cases, the progestative nomegestrol was added to estrogens (days 17 to 28 of the cycle). Lipoprotein parameters were evaluated after sepg. very-low-d. lipoproteins (VLDLs) by ultracentrifugation, while fasting glucose and insulin, homocysteine, and hemo-coagulative parameters were detd. in plasma. Fifty-four patients completed the trial. Total cholesterol (TC) and LDL-C significantly decreased in the simvastatin (-62 mg/dL [-20%] and -72 mg/dL [-30%], resp.), CEE (-42 mg/dL [-13%] and -45 mg/dL [-18%]), and ETP (-30 mg/dL [-10%] and -26 mg/dL [-11%]) groups compared to baseline, but only simvastatin showed an effect significantly superior to diet alone. Apolipoprotein (Apo) B was decreased by simvastatin (-25%, P <.001) and by CEE (-10%, P <.05); again, simvastatin was more effective than either diet or ETP. Triglyceride concn. and VLDL-C were unmodified by treatments. HDL-C and Apo A-I significantly increased in the simvastatin group (+18% and +8%, resp.), while HDL-C was unmodified by both HRT regimens and Apo A-I was reduced by ETP treatment (-17%); lipoprotein[a] (Lp[a]) was decreased by both HRTs (-38%, P <.05, and -22%, P =.07, for CEE and ETP, resp.). Among coagulative parameters, plasminogen activator inhibitor-1 (PAI-1) was significantly reduced by CEE (-29%, P <.05) but not ETP treatment (+16%, P = not significant), while fibrinogen, antithrombin, and homocysteine were unaffected by therapy. Thus, HRT, particularly CEE, seems well tolerated and moderately effective in improving the lipid pattern and, perhaps, the coagulative/fibrinolytic balance in postmenopausal hypercholesterolemic women; it may represent a therapeutic option in slightly dyslipidemic subjects. Statins are preferred in case of more severe disease.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:832625 CAPLUS
DOCUMENT NUMBER: 137:316114
TITLE: Novel hormone composition comprising a **estrogen** compound and a gestagenic compound
INVENTOR(S): Paris, Jacques; Thomas, Jean-Louis
PATENT ASSIGNEE(S): Laboratoire Theramex, Monaco
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

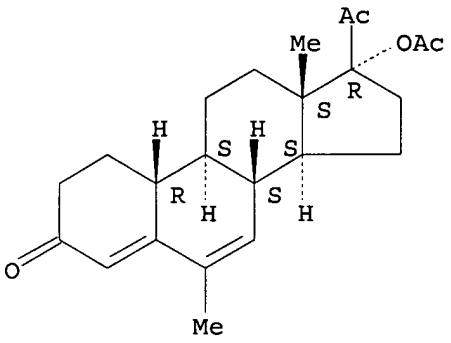
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085375	A1	20021031	WO 2002-FR1384	20020423

W: AE, AL, AU, BA, BG, BR, CA, CN, CO, CR, CU, CZ, DZ, EC, EE, HR, HU, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, RO, SG, SI, TN, US, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

09284147

FR 2823976 A1 20021031 FR 2001-5557 20010425
PRIORITY APPLN. INFO.: FR 2001-5557 A 20010425
IT **58652-20-3**, Nomegestrol acetate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel hormone compn. comprising **estrogen** compd. and gestagenic compd.)
RN 58652-20-3 CAPLUS
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

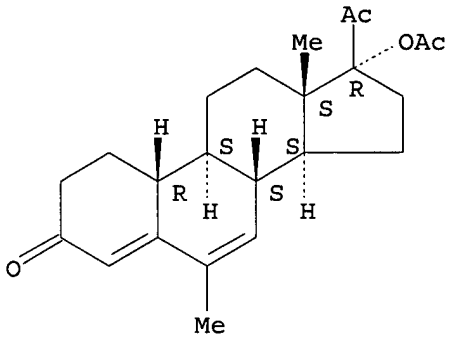


AB The invention relates to the field of therapeutic chem., more specifically to hormonal pharmaceutical techniques, esp. to novel hormonal pharmaceutical compns. which are formed as a result of an estro-gestagenic assocn. consisting of an **estrogen** compd. and a gestagenic compd., assocd. with or mixed with one or several non-toxic excipients which are inert and pharmaceutically acceptable and which can be administered orally. The invention also relates to the use of an estro-gestagenic mixt. wherein the estrogenic component and the gestagenic component are administered in a combined manner. Combined assocn. can be prescribed in a continuous or intermittent manner with a view to providing a compn. which can be used to treat estrogenic deficiency, and prevent osteoporosis and cardiovascular diseases in **menopause** women. The invention further relates to a method for the prodn. of said estro-gestagenic compns.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:495495 CAPLUS
DOCUMENT NUMBER: 137:195772
TITLE: Progestin effects on human endometrium in vitro
AUTHOR(S): Charpin, Colette; Illouz, Severine; Dales, Jean-Philippe; Lavaut, Marie-Noelle; Allasia, Claude; Boubli, Leon
CORPORATE SOURCE: Laboratoire d'Anatomie Pathologique, Faculte de Medecine Nord, Marseille, 13916, Fr.
SOURCE: Bulletin de l'Academie Nationale de Medecine (Paris, France) (2002), 186(1), 125-146
CODEN: BANMAC; ISSN: 0001-4079
PUBLISHER: Academie Nationale de Medecine
DOCUMENT TYPE: Journal
LANGUAGE: French
IT **58652-20-3**, Nomegestrol acetate

RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(progestin effects on human endometrium in vitro)
RN 58652-20-3 CAPLUS
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB In order to obtain a better evaluation of the epithelial proliferation of the human endometrium, we developed an "in vitro" model to quantify the effects of hormonal treatments, as an "hormonogram". We particularly aimed to evaluate the effects of steroids used in the replacement hormone therapy during **menopause** in the view of predicting and preventing the development of precancerous lesions of the endometrium. This study has evaluated the effects of different progestins currently used in hormone therapy, progesterone, medroxy-progesterone acetate (MPA), nomegestrol acetate (TX), norethindrone acetate (NOR) on human proliferative endometrium explant culture, using two means: prostaglandin F2.alpha. (PGF2.alpha.) output in medium culture, and immunoexpression of estradiol receptor (ER), progesterone receptor (PR) and proliferative antigen Ki67 in tissue. After culture, quant. studies on ER or PR immunoexpression could be assessed by image anal. procedure in contrast to Ki67 immunoexpression too weak low in non tumorous endometrium to be quantified. PGF2.alpha. output, was decreased by progesterone, TX and MPA in both proliferative endometrium subtypes. With regards to receptor immunoexpression, progesterone only decreased PR expression in proliferative endometrium. PR immunoexpression in stromal cells was decreased by all progestins in homogeneous proliferative endometrium explants. TX decreased PR and ER expression in glands and stroma of homogeneous proliferative endometrium. MPA exhibited similar effects but only on heterogeneous proliferative endometrium. In brief, our results show that in vitro progestative treatment on endometrium reduced PGF2.alpha. output and decreased PR and/or ER immunoexpression, although the in vitro effects of each progestin were not similar and varied with the endometrium subtype (proliferative homogeneous or heterogeneous). This study opens new fields of research particularly to investigate the endometrial proliferative activity using explant culture.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:220377 CAPLUS
DOCUMENT NUMBER: 136:252498
TITLE: Novel topical oestroprogestational compositions with

systemic effect

INVENTOR(S): Gray, Georges; Villet, Bertrand; Paris, Jacques; Thomas, Jean-Louis
PATENT ASSIGNEE(S): Laboratoire Theramex Sam, Monaco
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022132	A2	20020321	WO 2001-FR2865	20010914
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
FR 2814074	A1	20020322	FR 2000-11791	20000915
AU 2001090026	A5	20020326	AU 2001-90026	20010914
BR 2001007216	A	20020709	BR 2001-7216	20010914
EP 1265617	A2	20021218	EP 2001-969895	20010914
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NO 2002002292	A	20020715	NO 2002-2292	20020514

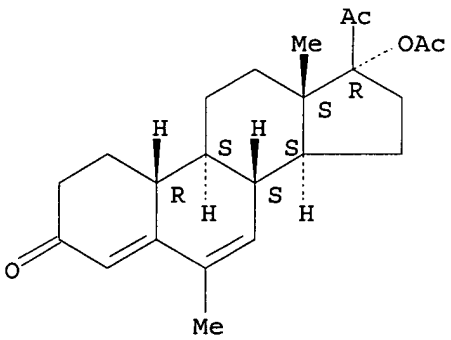
PRIORITY APPLN. INFO.: FR 2000-11791 A 20000915
WO 2001-FR2865 W 20010914

IT **58652-20-3**, Nomegestrol acetate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel topical oestroprogestational compns. with systemic effect)

RN 58652-20-3 CAPLUS

CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

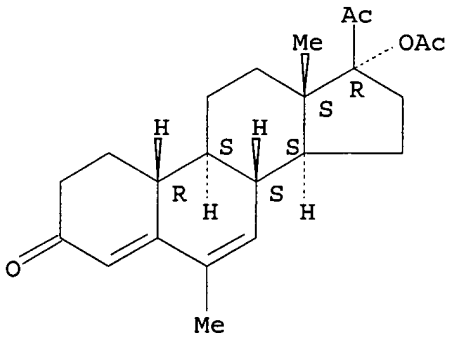


AB The invention concerns the field of therapeutic chem. and more particularly the prodn. of novel galenic forms to be applied on the skin. More particularly, it concerns a topical hormonal compn. with systemic effect for hormonal treatment of perimenopause and **menopause** as

well as for treating ovarian hormonal deficiency in a woman suffering from amenorrhea. The invention is characterized in that it comprises, as active principles, a progestational deriv. of the 19-norprogesterone and estradiol or one of its derivs., a carrier for systemic delivery of said active principles, selected among the group consisting of a film-forming agent, a gelling agent and mixts. thereof, combined with a mixt. of excipients suited for producing a gelled and/or film-forming pharmaceutical form. A topical gel contained nomegestrol acetate 0.4, estradiol 0.1, Carbopol-1342 0.5, propylene glycol 6, transcutol 5, EDTA 0.05, triethanolamine 0.3, water 42.65, and ethanol 45%. Effectiveness of the compn. was tested in female volunteers.

L20 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:856712 CAPLUS
DOCUMENT NUMBER: 136:178101
TITLE: Effects of different types of hormone replacement therapy on mammographic density
AUTHOR(S): Colacurci, Nicola; Fornaro, Felice; De Franciscis, Pasquale; Palermo, Mario; del Vecchio, Walter
CORPORATE SOURCE: Outpatient Menopausal Clinic, Institute of Gynaecology and Obstetrics, School of Medicine, Second University of Naples, Naples, 80134, Italy
SOURCE: Maturitas (2001), 40(2), 159-164
CODEN: MATUDK; ISSN: 0378-5122
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **58652-20-3**, Nomegestrol acetate
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of different types of hormone replacement therapy on mammog. d.)
RN 58652-20-3 CAPLUS
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



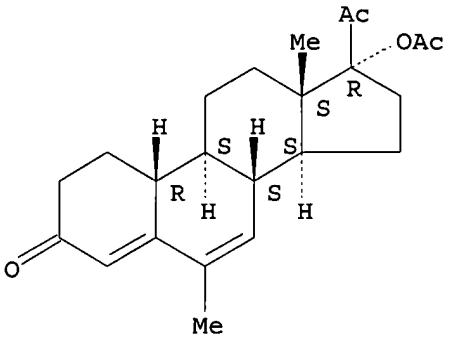
AB Objectives: to evaluate the effects of different types of hormone replacement therapy (HRT) on mammog. d. in postmenopausal women. Methods: In a prospective 1-yr study, 121 healthy postmenopausal women were allocated to one of the following five study groups: twenty-six women were treated with continuous transdermal 17beta-estradiol 50 mcg/die plus acetate nomegestrol 5 mg/die sequentially added for 12 days per mo (Group A); 25 women were treated with continuous transdermal 17beta-estradiol 50

mcg/die plus acetate nomegestrol 2.5 mg/die added every day (Group B); 23 women were treated with continuous transdermal 17beta-estradiol 50 mcg/die (Group C); 24 women were treated with tibolone 2.5 mg/die (Group D); and 23 women not receiving any medication represented the control group (Group E). At the time of recruitment and after 12 mo a two-view mammog. was performed to evaluate mammog. d. according to a quant. method: type 1 (less than 25% of mammary gland covered by dense tissue), type 2 (from 25 to 75% of total glandular area covered by dense tissue), type 3 (more than 75% of mammary parenchyma covered by dense tissue). Results: After 12 mo of HRT, seven out of 20 patients (35%) in group A, nine of 21 patients (42.85%) in group B, four out of 19 patients (21%) in group C and two of 20 patients (10%) in group D, showed an increase in mammog. d. No variation of d. was obsd. at the second mammog. test in the control group. The mammog. d. increase which occurred in groups A, B and C was statistically significant ($P<0.05$) when compared with group E; no statistically significant difference ($P=0.49$) was found in mammog. d. increase between group D and group E. When the different treatment types were compared each other, a statistically significant difference ($P=0.04$) was found only between the mammog. d. increase occurring in groups B and D. Conclusions: HRT may cause an increase of mammog. d. The frequency of the d. increase is related to the type of HRT and a replacement therapy including a progestin, esp. in continuous combination with **estrogen**, leads to more evident mammog. changes. Tibolone does not significantly affect mammog. d.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:566988 CAPLUS
DOCUMENT NUMBER: 135:327515
TITLE: Withdrawal of hormone replacement therapy is associated with significant vertebral bone loss in postmenopausal women
AUTHOR(S): Tremollieres, F. A.; Pouilles, J.-M.; Ribot, C.
CORPORATE SOURCE: Menopause and Bone Metabolic Disease Unit, CHU Rangueil, Toulouse, F-31403, Fr.
SOURCE: Osteoporosis International (2001), 12(5), 385-390
CODEN: OSINEP; ISSN: 0937-941X
PUBLISHER: Springer-Verlag London Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **58652-20-3**, Nomegestrol acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(withdrawal of hormone replacement therapy is assocd. with significant vertebral bone loss in postmenopausal women)
RN 58652-20-3 CAPLUS
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB This study aimed to assess the changes in vertebral bone mineral d. (BMD) after cessation of hormone replacement therapy (HRT) in postmenopausal women who had been treated on a long-term basis. Fifty healthy postmenopausal women who had been followed both during the course of HRT and after cessation of treatment in our **menopause** clinic were included in this study. All women had started HRT within the first 3 yr after the postmenopause and had received HRT (either 1.5 mg/day of 17.beta.-estradiol given percutaneously or 50 .mu.g/day of 17.beta.-estradiol given as a transdermal patch, combined in all women with natural progesterone or a 19-norprogesterone deriv.) for a mean 5.+-.2.4 yr. In all women, vertebral BMD was assessed during the course of HRT up to the last 6 mo before **estrogen** withdrawal, then at least once within the first 18 mo after cessation of treatment. Of the initial population, 30 women were addnl. reviewed later on and up to 8 yr after cessation of treatment (mean duration of follow-up for the whole population: 3.9.+-.1.7 yr). Rates of changes in vertebral BMD were compared with those detd. in a group of healthy untreated women who had been followed within the first years of postmenopause during the same time period as the study population. In the study group, bone loss was found to accelerate within the first 2 yr after HRT withdrawal and the annual rate of loss was identical to that which occurs within the first 2 yr of post-**menopause** in untreated women (-1.64% .+-. 1.3% vs. -1.52.+-.0.9%, NS). Beyond this first 2-yr time period, the annual rate of bone loss decreased as a function of time following cessation of treatment, as was obsd. following the **menopause** in untreated women (between 3 and 5 yr: -0.83% + 1.35% in the study group vs. -0.70% .+-. 0.8% in the control group, NS). On av., 3 yr after cessation of HRT mean vertebral BMD when expressed as a Z-score was significantly higher (-0.13 vs. -0.89, $p<0.01$) than at baseline, before HRT was started, which suggested a lasting beneficial effect on bone mass. However, even though our findings do not support the hypothesis that bone loss might continue to be accelerated several years after cessation of treatment we cannot fully address the question as to whether any residual benefit on bone mass over a longer period of time may be obsd. In conclusion, the pattern of bone loss obsd. after cessation of **estrogen** therapy was found to be comparable to that which occurs in younger women within the first years after the **menopause**. Such a pattern needs to be kept in mind when the decision to stop HRT is taken, esp. in women who were given HRT to prevent osteoporosis. The issue of assessing their risk of fracture several years after cessation of treatment thus needs to be addressed.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:319731 CAPLUS

09284147

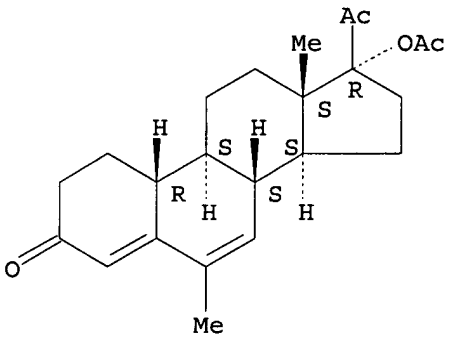
DOCUMENT NUMBER: 134:316160
TITLE: Hormonal composition based on a progestational agent and an **estrogen**
INVENTOR(S): Paris, Jacques; Thomas, Jean-Louis
PATENT ASSIGNEE(S): Laboratoire Theramex, Monaco
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001030356	A1	20010503	WO 1999-FR2588	19991025
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
WO 2001030357	A1	20010503	WO 2000-FR2939	20001024
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1227814	A1	20020807	EP 2000-971476	20001024
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
NO 2002001949	A	20020425	NO 2002-1949	20020425

PRIORITY APPLN. INFO.: WO 1999-FR2588 W 19991025
WO 2000-FR2939 W 20001024

IT **58652-20-3**, Nomegestrol acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hormonal compn. based on progestational agent and **estrogen**)
RN 58652-20-3 CAPLUS
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



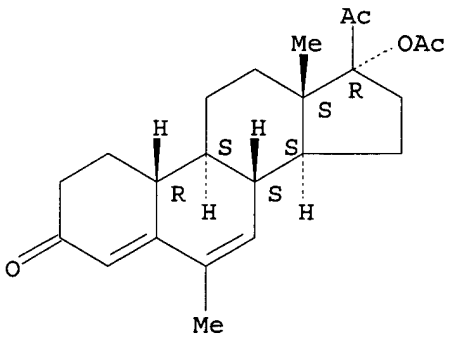
AB The invention concerns the field of therapeutic chem. and more

particularly the field of hormonal pharmaceutics technique. More precisely, it concerns novel hormonal compns. formed by an progestogen-**estrogen** combination consisting of an **estrogen** compd. and a progestational compd., assocd. or mixed with one or several pharmaceutically acceptable inert non-toxic carriers designed for oral administration. The invention also concerns the use of the progestogen-**estrogen** mixt. wherein the **estrogen** constituent and the progestogen constituent are administered in combination. The combined assocn. can be prescribed continuously or intermittently, so as to produce a compn. for treating **estrogen** deficiencies, preventing osteoporosis and cardiovascular diseases in postmenopausal women. The invention further concerns a method for prepg. said novel pharmaceutical progestogen-**estrogen** compns. A tablet contained estradiol 0.811, nomegestrol acetate 0.338, lactose 71.238, cellulose 15.032, povidone 7.297, Precirol AT05 1.503, colloidal silica 0.540, and crospovidone 3.243%. Antimitotic effects of the compn. in endometrial cells was studied.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:854101 CAPLUS
DOCUMENT NUMBER: 134:37255
TITLE: Nomegestrol acetate and vascular reactivity: nonhuman primate experiments
AUTHOR(S): Paris, J. M.; Williams, K. J.; Hermsmeyer, K. R.; Delansorne, R.
CORPORATE SOURCE: BP 59, Laboratoire Theramex, 98007, Monaco
SOURCE: Steroids (2000), 65(10-11), 621-627
CODEN: STEDAM; ISSN: 0039-128X
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **58652-20-3**, Nomegestrol acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(nomegestrol acetate and vascular reactivity in nonhuman primates in relation to role of progestins in hormone replacement therapy)
RN 58652-20-3 CAPLUS
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



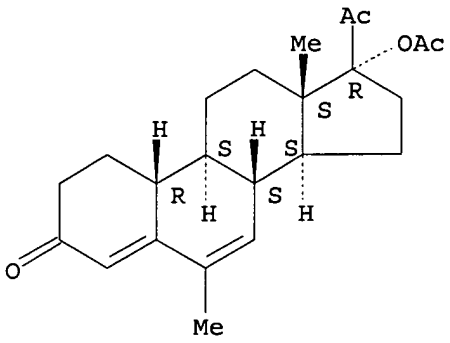
AB Prevention of coronary artery disease has been recognized as a major

benefit of **estrogen** replacement therapy (ERT) in postmenopausal women. However, endometrial hyperplasia induced by unopposed ERT has raised important safety concerns. Progesterone or synthetic progestins have been used in combined hormone replacement therapy (HRT) to prevent endometrial cancer risk. Therefore, a major concern has been to ensure that the vascular beneficial effects of estrogens are not opposed when combined with progestins. Nomegestrol acetate (NOMAC) is an orally active progestin widely prescribed for HRT. Its vascular effects were evaluated in two models of coronary vascular reactivity in primates: the paradoxical vasoconstriction to acetylcholine (Ach) coronary infusion after 5 mo of mildly atherogenic diet in ovariectomized (OVX) Cynomolgus monkeys and the pharmacol. evoked coronary vasospasm in the OVX Rhesus monkey. In the first model, after 3 mo of continuous oral administration in the diet at 0.1 mg/kg/day, E2 prevented the paradoxical response to Ach, alone as well as combined with 0.25 mg/kg/day NOMAC, whereas NOMAC counteracted the endometrial stimulation. In the second model, after one artificial cycle consisting of 28 days of E2 s.c. implant and of daily oral gavage with 1 mg/kg/day of NOMAC for the last 14 days, no vasospasm (0 of 11 tested animals) occurred when the complete challenge protocol, including serotonin and the thromboxane agonist U46619, was administered to OVX Rhesus monkeys. In the balanced crossover design, identical artificial cycles with medroxyprogesterone acetate (MPA) at the same dose resulted in 7 vasospasms in 12 animals. In parallel, effective progestative activity was demonstrated by a secretory pattern in endometrial sections obtained at the end of the cycle. In these two nonhuman primate cardiovascular models, NOMAC did not have the negating effects obsd. with MPA.

REFERENCE COUNT: 93 THERE ARE 93 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:790272 CAPLUS
DOCUMENT NUMBER: 130:177698
TITLE: Continuous hormone replacement therapy for **menopause** combining nomegestrol acetate and gel, patch, or oral **estrogen**: A comparison of amenorrhea rates
AUTHOR(S): Blanc, Bernard; Cravello, Ludovic; Micheletti, Marie-Christine; d'Ercole, Claude; Zartarian, Marie
CORPORATE SOURCE: Service de Gynecologie Obstetrique B, Hopital de la Conception, Marseille, Fr.
SOURCE: Clinical Therapeutics (1998), 20(5), 901-912
CODEN: CLTHDG; ISSN: 0149-2918
PUBLISHER: Excerpta Medica
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **58652-20-3**, Nomegestrol acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amenorrhea rates in continuous hormone replacement therapy combining nomegestrol acetate and gel, patch, or oral **estrogen** in **menopause** in women)
RN 58652-20-3 CAPLUS
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB This open-label, prospective, randomized, multicenter trial compared the incidence of amenorrhea in 54 postmenopausal women (mean age, 54.9 yr) who underwent six 4-wk cycles of continuous hormone replacement therapy combining a progestin-nomegestrol acetate 2.5 mg/d-plus one of three estrogens: percutaneous 17.beta.-estradiol gel (1.5 mg/d, group A), transdermal 17.beta.-estradiol patch (50 .mu.g/d, group B), or oral estradiol valerate (2 mg/d, group C). Based on an intent-to-treat anal., the rate of amenorrhea varied significantly according to which **estrogen** prepn. was used. Calcd. cycle by cycle, rates of amenorrhea were 67% to 83% for group A, 25% to 56% for group B, and 53% to 61% for group C. Overall rates of persistent amenorrhea were not statistically different between groups for cycles 1 through 3, but for cycles 4 through 6, significantly more women in groups A and C (67% and 46%, resp.) experienced amenorrhea than did those in group B (12%). Amenorrhea rates for the entire six-cycle period were 78% for group A, 48% for group B, and 60% for group C. These differences were not statistically significant. The differences in rates could not be attributed to endometrial atrophy, since when measured by transvaginal sonog., endometrial thickness did not differ significantly between groups. Of the original population, 7% withdrew prematurely because of bleeding. The data for all three groups confirmed that in two out of three women, the occurrence of amenorrhea during the first three cycles predicted continuation of amenorrhea during subsequent cycles and that for 51% of women, .ltoreq.10 days of bleeding during the first three cycles predicted amenorrhea during the last three cycles. Calcd. as a function of the no. of women included in the trial, the percentage of amenorrheic women (evaluated cycle by cycle or for the second three-cycle period) was highest when the progestin was combined with percutaneous 17.beta.-estradiol gel, although findings were similar with estradiol valerate. The percutaneous 17.beta.-estradiol gel was also assocd. with a higher percentage of amenorrheal cycles than was estradiol valerate or transdermal **estrogen**, although differences were significant only in comparison with the transdermal formulation. This difference may have pos. clin. implications.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:239116 CAPLUS
DOCUMENT NUMBER: 128:312905
TITLE: Pharmaceutical composition consisting of an **estrogen** and a progestogen
INVENTOR(S): Lanquetin, Michel; Paris, Jacques; Thomas, Jean-Louis
PATENT ASSIGNEE(S): Laboratoire Theramex, Monaco; Lanquetin, Michel; Paris, Jacques; Thomas, Jean-Louis

09284147

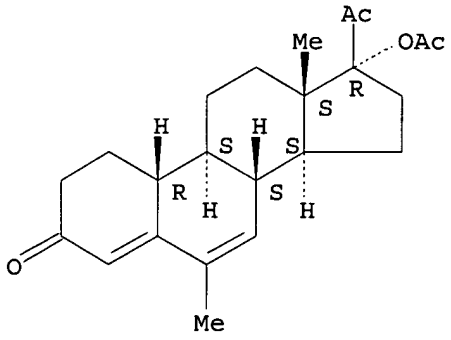
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9815279	A1	19980416	WO 1997-FR1792	19971008
W: AU, BR, CA, CN, CU, CZ, HU, ID, IL, JP, KR, MG, MX, NO, NZ, PL, RO, RU, SG, SK, TR, US, VN, YU				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2754179	A1	19980410	FR 1996-12239	19961008
FR 2754179	B1	19981224		
AU 9746273	A1	19980505	AU 1997-46273	19971008
AU 745571	B2	20020321		
ZA 9709011	A	19980603	ZA 1997-9011	19971008
BR 9712274	A	19990831	BR 1997-12274	19971008
EP 956022	A1	19991117	EP 1997-944940	19971008
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1239893	A	19991229	CN 1997-180380	19971008
JP 2002509524	T2	20020326	JP 1998-517263	19971008
NO 9901593	A	19990607	NO 1999-1593	19990331
MX 9903291	A	20000131	MX 1999-3291	19990408
KR 2000048981	A	20000725	KR 1999-703032	19990408

PRIORITY APPLN. INFO.: FR 1996-12239 A 19961008
WO 1997-FR1792 W 19971008

IT **58652-20-3**, Nomegestrol acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compn. consisting of an **estrogen** compd. and of a progestogen)
RN 58652-20-3 CAPLUS
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB The invention concerns the field of chem. therapy and more particularly the field of pharmaceutical hormonal technique. More precisely it

concerns novel pharmaceutical hormonal compns. characterized in that they are formed by an **estrogen**-progestogen combination assocd. or mixed with 1 or several nontoxic, inert and excipients, for oral administration. The combined assocn. can be prescribed continuously or intermittently, for producing a compn. for treating estrogenic deficiencies, preventing osteoporosis and cardiovascular diseases in menopausal women, or still for blocking ovulation in a woman during the period of ovarian activity. Thus, tablets contained estradiol 1.5, nomegestrol acetate 2.5, Avicel PH-102 22.4, lactose 60, PVP 8.4, colloidal silica 1.2, glycerol palmitostearate 3.6, and dye 0.4 mg. The effectiveness of this combination in the treatment of diseases in menopausal women was demonstrated.

L20 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:226799 CAPLUS
DOCUMENT NUMBER: 126:216684
TITLE: Novel hormonal medicaments and use thereof for correcting **estrogen** deficiencies
INVENTOR(S): Lanquetin, Michel; Paris, Jacques; Thomas, Jean-Louis
PATENT ASSIGNEE(S): Laboratoire Theramex, Monaco; Lanquetin, Michel; Paris, Jacques; Thomas, Jean-Louis
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

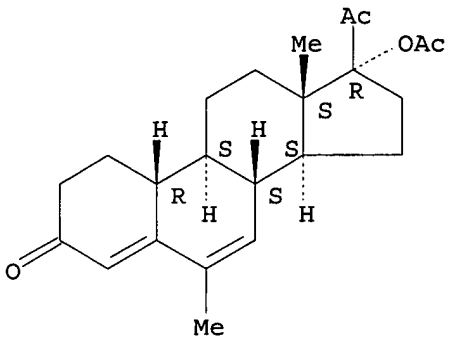
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9704784	A1	19970213	WO 1996-IB754	19960729
W: AU, BR, CA, CN, CZ, FI, HU, IL, JP, KR, MX, NO, RU, SG, US, VN				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2737411	A1	19970207	FR 1995-9364	19950801
FR 2737411	B1	19971017		
CA 2201368	AA	19970213	CA 1996-2201368	19960729
AU 9663674	A1	19970226	AU 1996-63674	19960729
AU 722355	B2	20000727		
EP 783310	A1	19970716	EP 1996-923018	19960729
EP 783310	B1	20021009		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1167438	A	19971210	CN 1996-191100	19960729
BR 9606549	A	19980623	BR 1996-6549	19960729
JP 10507207	T2	19980714	JP 1996-507406	19960729
CZ 289706	B6	20020313	CZ 1997-967	19960729
RU 2188641	C2	20020910	RU 1997-108279	19960729
AT 225659	E	20021015	AT 1996-923018	19960729
ZA 9606545	A	19970508	ZA 1996-6545	19960801
TW 473390	B	20020121	TW 1996-85111673	19960924
NO 9701449	A	19970530	NO 1997-1449	19970326
US 5891867	A	19990406	US 1997-817329	19970424

PRIORITY APPLN. INFO.: FR 1995-9364 A 19950801
WO 1996-IB754 W 19960729

IT **58652-20-3**, Nomegestrol acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)
(novel hormonal medicaments for correcting **estrogen** deficiencies)
RN 58652-20-3 CAPLUS
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

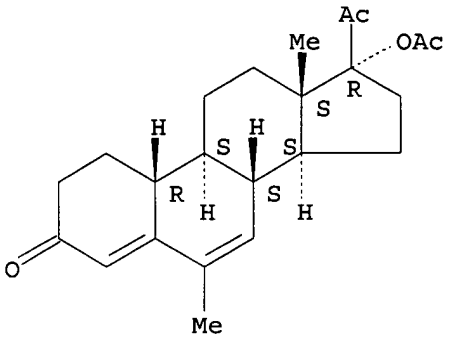


AB A trisequential, oestroprogestogen hormonal combination characterized in that it comprises unit doses contg. only one **estrogen**, unit doses contg. a combination of one **estrogen** and one progestogen, and unit doses contg. only one carrier. The trisequential delivery mode aims at compensating functional disorders caused by menopausal or pre-menopausal hypoestrogenism. Formulation of 1.5 mg 17.beta.-estradiol tablets and 2.5 mg nomegestrol acetate tablets are disclosed. The efficacy of tablets in treatment of hot flashes in menopausal women are reported.

=> d l18 ibib hitstr abs

L18 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:135333 CAPLUS
DOCUMENT NUMBER: 136:380208
TITLE: Nonmenstrual adverse events during use of implantable contraceptives for **women**: data from clinical trials
AUTHOR(S): Brache, V.; Faundes, A.; Alvarez, F.; Cochon, L.
CORPORATE SOURCE: PROFAMILIA, Santo Domingo, Dominican Rep.
SOURCE: Contraception (2002), 65(1), 63-74
CODEN: CCPTAY; ISSN: 0010-7824
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
IT **58652-20-3**, Uniplant
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nonmenstrual adverse events during use of implantable contraceptives for **women**)
RN 58652-20-3 CAPLUS
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB A review of the incidences of headache, wt. gain, acne, hair loss, hirsutism, dizziness, moot changes, nervousness, depression, nausea, breast tenderness, loss of libido, fatigue, lower abdominal pain, and ovarian cysts in **women** using several progestogen contraceptive implants, Norplant, Jadelle, Implanon, and Uniplant.

REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=>

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```
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
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FILE 'HOME' ENTERED AT 15:30:47 ON 09 JAN 2003

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

FILE 'REGISTRY' ENTERED AT 15:30:52 ON 09 JAN 2003
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STRUCTURE FILE UPDATES:     8 JAN 2003  HIGHEST RN 478480-50-1
DICTIONARY FILE UPDATES:    8 JAN 2003  HIGHEST RN 478480-50-1

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> s nomegesterol acetate
             0 NOMEGESTEROL
        431171 ACETATE
L1           0 NOMEGESTEROL ACETATE
                 (NOMEGESTEROL(W)ACETATE)

=> s nomegestrol acetate
             2 NOMEGESTROL
        431171 ACETATE
L2           1 NOMEGESTROL ACETATE
                 (NOMEGESTROL(W)ACETATE)

=> d l2
```
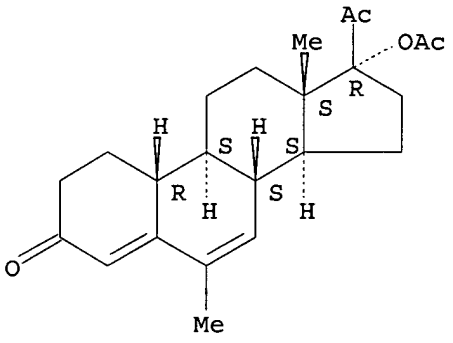

09284147

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS
RN 58652-20-3 REGISTRY
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 6-Methyl-17.alpha.-acetoxy-.DELTA.6-19-norprogesterone
CN Lutenyl
CN **Nomegestrol acetate**
CN Surplant
CN TX 066
CN Uniplant
FS STEREOSEARCH
MF C23 H30 O4
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CHEMLIST, CIN, DDFU, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, PHAR, PHARMASEARCH, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

78 REFERENCES IN FILE CA (1962 TO DATE)
78 REFERENCES IN FILE CAPLUS (1962 TO DATE)

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	19.76	19.97

FILE 'REGISTRY' ENTERED AT 15:32:41 ON 09 JAN 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

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STRUCTURE FILE UPDATES: 8 JAN 2003 HIGHEST RN 478480-50-1
DICTIONARY FILE UPDATES: 8 JAN 2003 HIGHEST RN 478480-50-1

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

```
=> s l1
             0 NOMEGESTEROL
        431171 ACETATE
L3           0 NOMEGESTEROL ACETATE
                 (NOMEGESTEROL(W)ACETATE)

=> s l2
             2 NOMEGESTROL
        431171 ACETATE
L4           1 NOMEGESTROL ACETATE
                 (NOMEGESTROL(W)ACETATE)

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'IBIB' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'
'HITSTR' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'
'ABS' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'
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The following are valid formats:

Substance information can be displayed by requesting individual fields or predefined formats. The predefined substance formats are: (RN = CAS Registry Number)

```
REG     - RN
SAM     - Index Name, MF, and structure - no RN
FIDE    - All substance data, except sequence data
IDE     - FIDE, but only 50 names
SQIDE   - IDE, plus sequence data
SQIDE3  - Same as SQIDE, but 3-letter amino acid codes are used
SQD     - Protein sequence data, includes RN
SQD3    - Same as SQD, but 3-letter amino acid codes are used
SQN     - Protein sequence name information, includes RN

CALC    - Table of calculated properties
EPROP   - Table of experimental properties
PROP    - EPROP and CALC
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Any CA File format may be combined with any substance format to obtain CA references citing the substance. The substance formats must be cited first. The CA File predefined formats are:

```
ABS  -- Abstract
APPS -- Application and Priority Information
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09284147

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BIB  -- CA Accession Number, plus Bibliographic Data
CAN  -- CA Accession Number
CBIB -- CA Accession Number, plus Bibliographic Data (compressed)
IND  -- Index Data
IPC  -- International Patent Classification
PATS -- PI, SO
STD  -- BIB, IPC, and NCL

IABS --ABS, indented, with text labels
IBIB -- BIB, indented, with text labels
ISTD -- STD format, indented

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

The ALL format gives FIDE BIB ABS IND RE, plus sequence data when
it is available.
The MAX format is the same as ALL.
The IALL format is the same as ALL with BIB ABS and IND indented,
with text labels.

For additional information, please consult the following help
messages:

HELP DFIELDS -- To see a complete list of individual display fields.
HELP FORMATS -- To see detailed descriptions of the predefined formats.
ENTER DISPLAY FORMAT (IDE):end

=> d his

     (FILE 'HOME' ENTERED AT 15:30:47 ON 09 JAN 2003)

     FILE 'REGISTRY' ENTERED AT 15:30:52 ON 09 JAN 2003
L1            0 S NOMEGESTEROL ACETATE
L2            1 S NOMEGESTROL ACETATE

     FILE 'REGISTRY' ENTERED AT 15:32:41 ON 09 JAN 2003
L3            0 S L1
L4            1 S L2

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                18.08      38.05

FILE 'CAPLUS' ENTERED AT 15:34:27 ON 09 JAN 2003
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```

FILE COVERS 1907 - 9 Jan 2003 VOL 138 ISS 2
FILE LAST UPDATED: 8 Jan 2003 (20030108/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

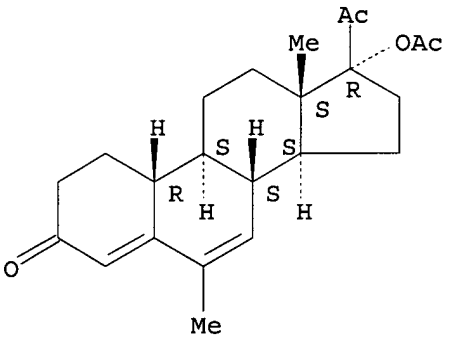
CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

```
=> s l4
L5          78 L4

=> d his

     (FILE 'HOME' ENTERED AT 15:30:47 ON 09 JAN 2003)

     FILE 'REGISTRY' ENTERED AT 15:30:52 ON 09 JAN 2003
L1            0 S NOMEGESTEROL ACETATE
L2            1 S NOMEGESTROL ACETATE

     FILE 'REGISTRY' ENTERED AT 15:32:41 ON 09 JAN 2003
L3            0 S L1
L4            1 S L2

     FILE 'CAPLUS' ENTERED AT 15:34:27 ON 09 JAN 2003
L5           78 S L4

=> s l2
L6          78 L2

=> s l6 and estrogen
         60689 ESTROGEN
L7          22 L6 AND ESTROGEN

=> s l7 and treatment
       1731757 TREATMENT
L8           9 L7 AND TREATMENT

=> d l8 1-9 ibib hitstr abs

L8   ANSWER 1 OF 9  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:        2002:859068  CAPLUS
DOCUMENT NUMBER:         137:362854
TITLE:                   Simvastatin, transdermal patch, and oral
                         estrogen-progestogen preparation in
                         early-postmenopausal hypercholesterolemic women: a
                         randomized, placebo-controlled clinical trial
AUTHOR(S):               Vigna, Giovanni B.; Donega, Paola; Zanca, Rosanna;
                         Barban, Angela; Passaro, Angelina; Pansini, Francesco;
                         Bonaccorsi, Gloria; Mollica, Gioacchino; Fellin,
                         Renato
CORPORATE SOURCE:        Department of Clinical and Experimental Medicine,
```

09284147

Section of Internal Medicine II, University of Ferrara, Ferrara, 44100, Italy
SOURCE: Metabolism, Clinical and Experimental (2002), 51(11), 1463-1470
CODEN: METAAJ; ISSN: 0026-0495
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **58652-20-3**, Nomegestrol acetate
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(simvastatin transdermal patch and oral **estrogen**-progestogen prepn. in early-postmenopausal hypercholesterolemic women)
RN 58652-20-3 CAPLUS
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Hormone replacement therapy (HRT) seems to have a favorable influence on the plasma lipid profile. Only a few investigations have examd. the effects of HRT vs. hepatic hydroxymethyl glutaryl CoA (HMG-CoA) reductase inhibitors. We compared the relative effects of different hypolipidemic strategies on lipoproteins and coagulative parameters in women with recent-onset spontaneous menopause. In this 24-wk, placebo-controlled trial, 60 consecutive healthy women aged .gtoreq. 45 yr, with amenorrhea from 6 to 60 mo (mean, 1.9.+-.1.4 yr), serum FSH greater than 40 U/L, and slight to moderate hypercholesterolemia (low-d. lipoprotein-cholesterol [LDL-C] 160 to 250 mg/dL, high-d. lipoprotein-cholesterol [HDL-C] < 75 mg/dL, and triglycerides < 200 mg/dL) were enrolled and randomized to dietetic advice (placebo group), simvastatin 10 mg, 0.625 mg of conjugated equine **estrogen** (CEE), or 50 .mu.g **estrogen** transdermal patch (ETP). In the latter 2 cases, the progestative nomegestrol was added to estrogens (days 17 to 28 of the cycle). Lipoprotein parameters were evaluated after sepg. very-low-d. lipoproteins (VLDLs) by ultracentrifugation, while fasting glucose and insulin, homocysteine, and hemo-coagulative parameters were detd. in plasma. Fifty-four patients completed the trial. Total cholesterol (TC) and LDL-C significantly decreased in the simvastatin (-62 mg/dL [-20%] and -72 mg/dL [-30%], resp.), CEE (-42 mg/dL [-13%] and -45 mg/dL [-18%]), and ETP (-30 mg/dL [-10%] and -26 mg/dL [-11%]) groups compared to baseline, but only simvastatin showed an effect significantly superior to diet alone. Apolipoprotein (Apo) B was decreased by simvastatin (-25%, P <.001) and by CEE (-10%, P <.05); again, simvastatin was more effective than either diet or ETP. Triglyceride concn. and VLDL-C were unmodified by treatments.

HDL-C and Apo A-I significantly increased in the simvastatin group (+18% and +8%, resp.), while HDL-C was unmodified by both HRT regimens and Apo A-I was reduced by ETP **treatment** (-17%); lipoprotein[a] (Lp[a]) was decreased by both HRTs (-38%, P <.05, and -22%, P =.07, for CEE and ETP, resp.). Among coagulative parameters, plasminogen activator inhibitor-1 (PAI-1) was significantly reduced by CEE (-29%, P <.05) but not ETP **treatment** (+16%, P = not significant), while fibrinogen, antithrombin, and homocysteine were unaffected by therapy. Thus, HRT, particularly CEE, seems well tolerated and moderately effective in improving the lipid pattern and, perhaps, the coagulative/fibrinolytic balance in postmenopausal hypercholesterolemic women; it may represent a therapeutic option in slightly dyslipidemic subjects. Statins are preferred in case of more severe disease.

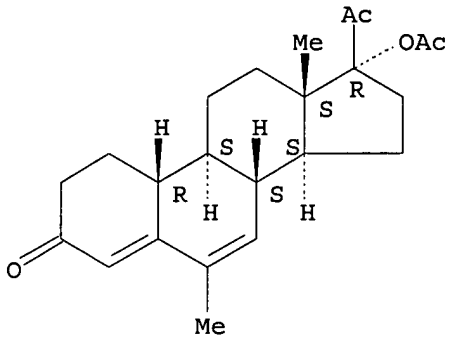
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:504629 CAPLUS
DOCUMENT NUMBER: 137:83634
TITLE: **Estrogen**, androgen and vasodilator compositions for the **treatment** of female sexual dysfunction
INVENTOR(S): Leonard, Thomas W.; Waldon, R. Waldon
PATENT ASSIGNEE(S): Endeavor Pharmaceuticals, USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002051420	A2	20020704	WO 2001-US49978	20011221
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002107230	A1	20020808	US 2001-29423	20011220

PRIORITY APPLN. INFO.: US 2000-257745P P 20001222
IT **58652-20-3**, Nomegestrol acetate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**estrogen**, androgen and vasodilator compns. for the **treatment** of female sexual dysfunction)
RN 58652-20-3 CAPLUS
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

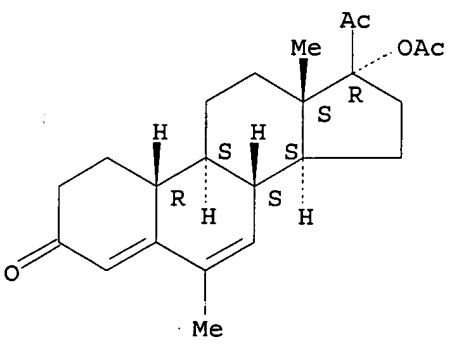
Absolute stereochemistry.

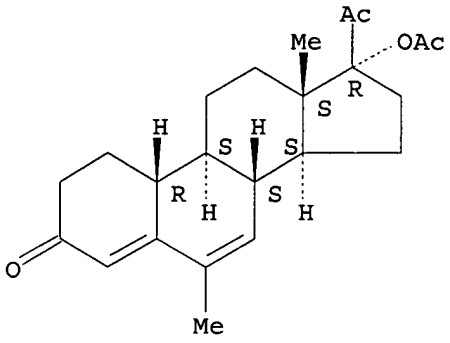


AB A pharmaceutical compn. for the **treatment** of sexual dysfunction, particularly post-menopausal females, is provided. The compn. includes a therapeutically effective amt. of an estrogenic compd., androgenic compd., vasodilation compd., and a pharmaceutically acceptable carrier. Tablets were prepd. contg. and **estrogen** such as estradiol, an androgen such as methyltestosterone and a vasodilator such as phentolamine and excipients.

L8 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:495495 CAPLUS
DOCUMENT NUMBER: 137:195772
TITLE: Progestin effects on human endometrium in vitro
AUTHOR(S): Charpin, Colette; Illouz, Severine; Dales, Jean-Philippe; Lavaut, Marie-Noelle; Allasia, Claude; Boubli, Leon
CORPORATE SOURCE: Laboratoire d'Anatomie Pathologique, Faculte de Medecine Nord, Marseille, 13916, Fr.
SOURCE: Bulletin de l'Academie Nationale de Medecine (Paris, France) (2002), 186(1), 125-146
CODEN: BANMAC; ISSN: 0001-4079
PUBLISHER: Academie Nationale de Medecine
DOCUMENT TYPE: Journal
LANGUAGE: French
IT **58652-20-3**, Nomegestrol acetate
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(progestin effects on human endometrium in vitro)
RN 58652-20-3 CAPLUS
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.





AB In order to obtain a better evaluation of the epithelial proliferation of the human endometrium, we developed an "in vitro" model to quantify the effects of hormonal treatments, as an "hormonogram". We particularly aimed to evaluate the effects of steroids used in the replacement hormone therapy during menopause in the view of predicting and preventing the development of precancerous lesions of the endometrium. This study has evaluated the effects of different progestins currently used in hormone therapy, progesterone, medroxy-progesterone acetate (MPA), nomegestrol acetate (TX), norethindrone acetate (NOR) on human proliferative endometrium explant culture, using two means: prostaglandin F2.alpha. (PGF2.alpha.) output in medium culture, and immunoexpression of estradiol receptor (ER), progesterone receptor (PR) and proliferative antigen Ki67 in tissue. After culture, quant. studies on ER or PR immunoexpression could be assessed by image anal. procedure in contrast to Ki67 immunoexpression too weak low in non tumorous endometrium to be quantified. PGF2.alpha. output, was decreased by progesterone, TX and MPA in both proliferative endometrium subtypes. With regards to receptor immunoexpression, progesterone only decreased PR expression in proliferative endometrium. PR immunoexpression in stromal cells was decreased by all progestins in homogeneous proliferative endometrium explants. TX decreased PR and ER expression in glands and stroma of homogeneous proliferative endometrium. MPA exhibited similar effects but only on heterogeneous proliferative endometrium. In brief, our results show that in vitro progestative **treatment** on endometrium reduced PGF2.alpha. output and decreased PR and/or ER immunoexpression, although the in vitro effects of each progestin were not similar and varied with the endometrium subtype (proliferative homogeneous or heterogeneous). This study opens new fields of research particularly to investigate the endometrial proliferative activity using explant culture.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:220377 CAPLUS
DOCUMENT NUMBER: 136:252498

TITLE: Novel topical oestroprogestational compositions with systemic effect

INVENTOR(S): Gray, Georges; Villet, Bertrand; Paris, Jacques; Thomas, Jean-Louis
PATENT ASSIGNEE(S): Laboratoire Theramex Sam, Monaco

SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1

09284147

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022132	A2	20020321	WO 2001-FR2865	20010914
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
FR 2814074	A1	20020322	FR 2000-11791	20000915
AU 2001090026	A5	20020326	AU 2001-90026	20010914
BR 2001007216	A	20020709	BR 2001-7216	20010914
EP 1265617	A2	20021218	EP 2001-969895	20010914
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NO 2002002292	A	20020715	NO 2002-2292	20020514

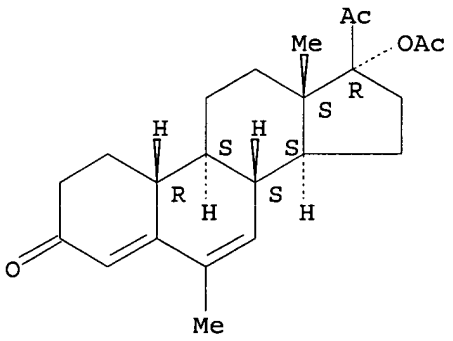
PRIORITY APPLN. INFO.: FR 2000-11791 A 20000915
WO 2001-FR2865 W 20010914

IT **58652-20-3**, Nomegestrol acetate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel topical oestroprogestational compns. with systemic effect)

RN 58652-20-3 CAPLUS

CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

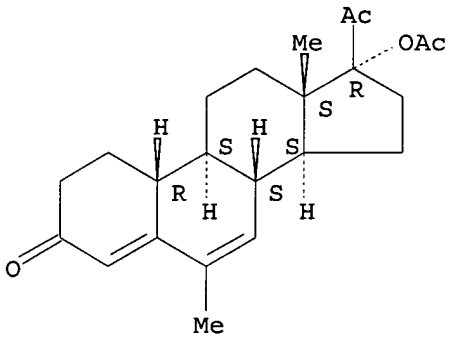


AB The invention concerns the field of therapeutic chem. and more particularly the prodn. of novel galenic forms to be applied on the skin. More particularly, it concerns a topical hormonal compn. with systemic effect for hormonal **treatment** of perimenopause and menopause as well as for treating ovarian hormonal deficiency in a woman suffering from amenorrhea. The invention is characterized in that it comprises, as active principles, a progestational deriv. of the 19-norprogesterone and estradiol or one of its derivs., a carrier for systemic delivery of said active principles, selected among the group consisting of a film-forming agent, a gelling agent and mixts. thereof, combined with a mixt. of excipients suited for producing a gelled and/or film-forming pharmaceutical form. A topical gel contained nomegestrol acetate 0.4, estradiol 0.1, Carbopol-1342 0.5, propylene glycol 6, transcutol 5, EDTA

0.05, triethanolamine 0.3, water 42.65, and ethanol 45%. Effectiveness of the compn. was tested in female volunteers.

L8 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:856712 CAPLUS
DOCUMENT NUMBER: 136:178101
TITLE: Effects of different types of hormone replacement therapy on mammographic density
AUTHOR(S): Colacurci, Nicola; Fornaro, Felice; De Franciscis, Pasquale; Palermo, Mario; del Vecchio, Walter
CORPORATE SOURCE: Outpatient Menopausal Clinic, Institute of Gynaecology and Obstetrics, School of Medicine, Second University of Naples, Naples, 80134, Italy
SOURCE: Maturitas (2001), 40(2), 159-164
CODEN: MATUDK; ISSN: 0378-5122
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **58652-20-3**, Nomegestrol acetate
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of different types of hormone replacement therapy on mammog. d.)
RN 58652-20-3 CAPLUS
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



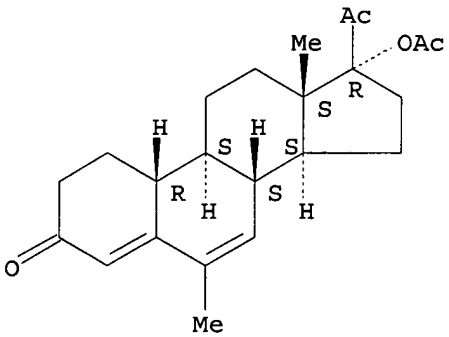
AB Objectives: to evaluate the effects of different types of hormone replacement therapy (HRT) on mammog. d. in postmenopausal women. Methods: In a prospective 1-yr study, 121 healthy postmenopausal women were allocated to one of the following five study groups: twenty-six women were treated with continuous transdermal 17beta-estradiol 50 mcg/die plus acetate nomegestrol 5 mg/die sequentially added for 12 days per mo (Group A); 25 women were treated with continuous transdermal 17beta-estradiol 50 mcg/die plus acetate nomegestrol 2.5 mg/die added every day (Group B); 23 women were treated with continuous transdermal 17beta-estradiol 50 mcg/die (Group C); 24 women were treated with tibolone 2.5 mg/die (Group D); and 23 women not receiving any medication represented the control group (Group E). At the time of recruitment and after 12 mo a two-view mammog. was performed to evaluate mammog. d. according to a quant. method: type 1 (less than 25% of mammary gland covered by dense tissue), type 2 (from 25 to 75% of total glandular area covered by dense tissue), type 3 (more than 75% of mammary parenchyma covered by dense tissue). Results: After 12 mo

of HRT, seven out of 20 patients (35%) in group A, nine of 21 patients (42.85%) in group B, four out of 19 patients (21%) in group C and two of 20 patients (10%) in group D, showed an increase in mammog. d. No variation of d. was obsd. at the second mammog. test in the control group. The mammog. d. increase which occurred in groups A, B and C was statistically significant ($P<0.05$) when compared with group E; no statistically significant difference ($P=0.49$) was found in mammog. d. increase between group D and group E. When the different **treatment** types were compared each other, a statistically significant difference ($P=0.04$) was found only between the mammog. d. increase occurring in groups B and D. Conclusions: HRT may cause an increase of mammog. d. The frequency of the d. increase is related to the type of HRT and a replacement therapy including a progestin, esp. in continuous combination with **estrogen**, leads to more evident mammog. changes. Tibolone does not significantly affect mammog. d.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:566988 CAPLUS
DOCUMENT NUMBER: 135:327515
TITLE: Withdrawal of hormone replacement therapy is associated with significant vertebral bone loss in postmenopausal women
AUTHOR(S): Tremollieres, F. A.; Pouilles, J.-M.; Ribot, C.
CORPORATE SOURCE: Menopause and Bone Metabolic Disease Unit, CHU Rangueil, Toulouse, F-31403, Fr.
SOURCE: Osteoporosis International (2001), 12(5), 385-390
CODEN: OSINEP; ISSN: 0937-941X
PUBLISHER: Springer-Verlag London Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **58652-20-3**, Nomegestrol acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(withdrawal of hormone replacement therapy is assocd. with significant vertebral bone loss in postmenopausal women)
RN 58652-20-3 CAPLUS
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB This study aimed to assess the changes in vertebral bone mineral d. (BMD)

after cessation of hormone replacement therapy (HRT) in postmenopausal women who had been treated on a long-term basis. Fifty healthy postmenopausal women who had been followed both during the course of HRT and after cessation of **treatment** in our menopause clinic were included in this study. All women had started HRT within the first 3 yr after the postmenopause and had received HRT (either 1.5 mg/day of 17.beta.-estradiol given percutaneously or 50 .mu.g/day of 17.beta.-estradiol given as a transdermal patch, combined in all women with natural progesterone or a 19-norprogesterone deriv.) for a mean 5.+-.2.4 yr. In all women, vertebral BMD was assessed during the course of HRT up to the last 6 mo before **estrogen** withdrawal, then at least once within the first 18 mo after cessation of **treatment**. Of the initial population, 30 women were addnl. reviewed later on and up to 8 yr after cessation of **treatment** (mean duration of follow-up for the whole population: 3.9.+-.1.7 yr). Rates of changes in vertebral BMD were compared with those detd. in a group of healthy untreated women who had been followed within the first years of postmenopause during the same time period as the study population. In the study group, bone loss was found to accelerate within the first 2 yr after HRT withdrawal and the annual rate of loss was identical to that which occurs within the first 2 yr of post-menopause in untreated women (-1.64% .+-. 1.3% vs. -1.52.+-.0.9%, NS). Beyond this first 2-yr time period, the annual rate of bone loss decreased as a function of time following cessation of **treatment**, as was obsd. following the menopause in untreated women (between 3 and 5 yr: -0.83% + 1.35% in the study group vs. -0.70% .+-. 0.8% in the control group, NS). On av., 3 yr after cessation of HRT mean vertebral BMD when expressed as a Z-score was significantly higher (-0.13 vs. -0.89, $p<0.01$) than at baseline, before HRT was started, which suggested a lasting beneficial effect on bone mass. However, even though our findings do not support the hypothesis that bone loss might continue to be accelerated several years after cessation of **treatment** we cannot fully address the question as to whether any residual benefit on bone mass over a longer period of time may be obsd. In conclusion, the pattern of bone loss obsd. after cessation of **estrogen** therapy was found to be comparable to that which occurs in younger women within the first years after the menopause. Such a pattern needs to be kept in mind when the decision to stop HRT is taken, esp. in women who were given HRT to prevent osteoporosis. The issue of assessing their risk of fracture several years after cessation of **treatment** thus needs to be addressed.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:787662 CAPLUS

DOCUMENT NUMBER: 130:163331

TITLE: Coadministration of nomegestrol acetate does not diminish the beneficial effects of estradiol on coronary artery dilator responses in nonhuman primates (Macaca fascicularis)

AUTHOR(S): Williams, J. Koudy; Cline, J. Mark; Honore, Erika K.; Delansorne, Remi; Paris, Jacques

CORPORATE SOURCE: Department of Comparative Medicine of Wake Forest, University School of Medicine, Winston-Salem, NC, 27157-1040, USA

SOURCE: American Journal of Obstetrics and Gynecology (1998), 179(5), 1288-1294
CODEN: AJOGAH; ISSN: 0002-9378

PUBLISHER: Mosby, Inc.

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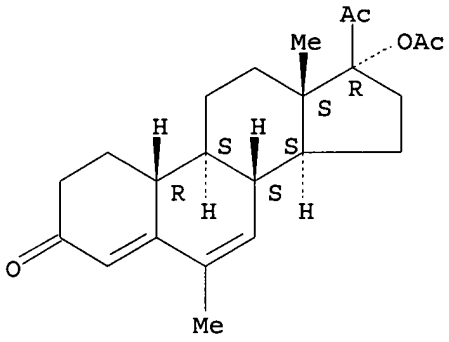
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **58652-20-3**, Nomegestrol acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nomegestrol acetate coadministration does not diminish estradiol beneficial effects on coronary artery dilator responses in nonhuman primates)
RN 58652-20-3 CAPLUS
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Our purpose was to examine the effect of coadministered nomegestrol acetate on estradiol-induced dilator responses of coronary arteries. In this prospective randomized trial, ovariectomized monkeys were fed a moderately atherogenic diet for 3 mo while being treated with (1) no hormone replacement (control), (2) estradiol (1.5 mg/d equiv.) added to the diet, or (3) estradiol (1.5 mg/d equiv.) plus nomegestrol acetate (3.75 mg/d equiv.) added to the diet. Effects of **treatment** were measured with anal. of variance. Post hoc analyses were done by multiple comparison tests with Bonferroni corrections. Constrictor responses of epicardial coronary arteries (measured with quant. angiog.) and decreased coronary blood velocity (measured with Doppler ultrasonog.) to acetylcholine (10-6 mol/L) were less in the estradiol-treated monkeys (with or without cotreatment with nomegestrol acetate) than in the untreated monkeys. Typical estrogenic responses were induced by estradiol in the endometrium (i.e., increased proliferation (Ki-67 expression) and increased hormone receptor expression). These effects were antagonized by nomegestrol acetate. Although nomegestrol acetate has typical progestin-like effects on the uterus, it does not diminish the beneficial effects of **estrogen** on acetylcholine-induced dilator responses of coronary arteries.
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:239116 CAPLUS
DOCUMENT NUMBER: 128:312905
TITLE: Pharmaceutical composition consisting of an **estrogen** and a progestogen
INVENTOR(S): Lanquetin, Michel; Paris, Jacques; Thomas, Jean-Louis
PATENT ASSIGNEE(S): Laboratoire Theramex, Monaco; Lanquetin, Michel;

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	Paris, Jacques; Thomas, Jean-Louis
SOURCE:	PCT Int. Appl., 22 pp.
	CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	French
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9815279	A1	19980416	WO 1997-FR1792	19971008
W: AU, BR, CA, CN, CU, CZ, HU, ID, IL, JP, KR, MG, MX, NO, NZ, PL, RO, RU, SG, SK, TR, US, VN, YU				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2754179	A1	19980410	FR 1996-12239	19961008
FR 2754179	B1	19981224		
AU 9746273	A1	19980505	AU 1997-46273	19971008
AU 745571	B2	20020321		
ZA 9709011	A	19980603	ZA 1997-9011	19971008
BR 9712274	A	19990831	BR 1997-12274	19971008
EP 956022	A1	19991117	EP 1997-944940	19971008
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1239893	A	19991229	CN 1997-180380	19971008
JP 2002509524	T2	20020326	JP 1998-517263	19971008
NO 9901593	A	19990607	NO 1999-1593	19990331
MX 9903291	A	20000131	MX 1999-3291	19990408
KR 2000048981	A	20000725	KR 1999-703032	19990408

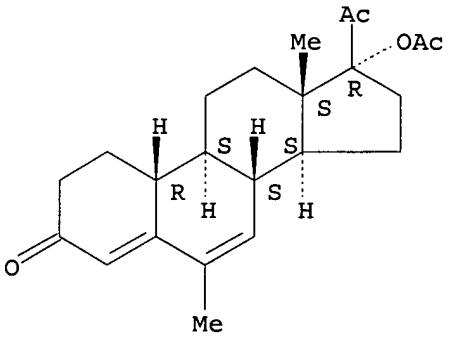
PRIORITY APPLN. INFO.:	FR 1996-12239	A	19961008
	WO 1997-FR1792	W	19971008

IT **58652-20-3**, Nomegestrol acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compn. consisting of an **estrogen** compd. and of a progestogen)

RN 58652-20-3 CAPLUS

CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB The invention concerns the field of chem. therapy and more particularly

the field of pharmaceutical hormonal technique. More precisely it concerns novel pharmaceutical hormonal compns. characterized in that they are formed by an **estrogen**-progestogen combination assocd. or mixed with 1 or several nontoxic, inert and excipients, for oral administration. The combined assocn. can be prescribed continuously or intermittently, for producing a compn. for treating estrogenic deficiencies, preventing osteoporosis and cardiovascular diseases in menopausal women, or still for blocking ovulation in a woman during the period of ovarian activity. Thus, tablets contained estradiol 1.5, nomegestrol acetate 2.5, Avicel PH-102 22.4, lactose 60, PVP 8.4, colloidal silica 1.2, glycerol palmitostearate 3.6, and dye 0.4 mg. The effectiveness of this combination in the **treatment** of diseases in menopausal women was demonstrated.

L8 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:226799 CAPLUS
DOCUMENT NUMBER: 126:216684
TITLE: Novel hormonal medicaments and use thereof for correcting **estrogen** deficiencies
INVENTOR(S): Lanquetin, Michel; Paris, Jacques; Thomas, Jean-Louis
PATENT ASSIGNEE(S): Laboratoire Theramex, Monaco; Lanquetin, Michel; Paris, Jacques; Thomas, Jean-Louis
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9704784	A1	19970213	WO 1996-IB754	19960729
W: AU, BR, CA, CN, CZ, FI, HU, IL, JP, KR, MX, NO, RU, SG, US, VN				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2737411	A1	19970207	FR 1995-9364	19950801
FR 2737411	B1	19971017		
CA 2201368	AA	19970213	CA 1996-2201368	19960729
AU 9663674	A1	19970226	AU 1996-63674	19960729
AU 722355	B2	20000727		
EP 783310	A1	19970716	EP 1996-923018	19960729
EP 783310	B1	20021009		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1167438	A	19971210	CN 1996-191100	19960729
BR 9606549	A	19980623	BR 1996-6549	19960729
JP 10507207	T2	19980714	JP 1996-507406	19960729
CZ 289706	B6	20020313	CZ 1997-967	19960729
RU 2188641	C2	20020910	RU 1997-108279	19960729
AT 225659	E	20021015	AT 1996-923018	19960729
ZA 9606545	A	19970508	ZA 1996-6545	19960801
TW 473390	B	20020121	TW 1996-85111673	19960924
NO 9701449	A	19970530	NO 1997-1449	19970326
US 5891867	A	19990406	US 1997-817329	19970424

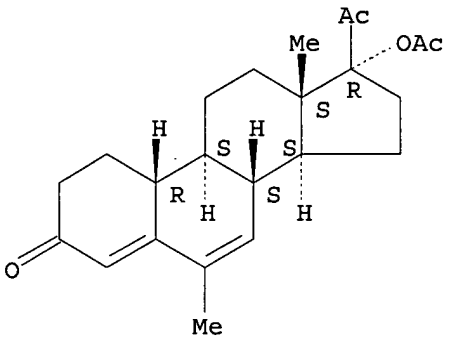
PRIORITY APPLN. INFO.: FR 1995-9364 A 19950801
WO 1996-IB754 W 19960729

IT **58652-20-3**, Nomegestrol acetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel hormonal medicaments for correcting **estrogen** deficiencies)

RN 58652-20-3 CAPLUS
CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetyloxy)-6-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB A trisequential, oestroprogestogen hormonal combination characterized in that it comprises unit doses contg. only one **estrogen**, unit doses contg. a combination of one **estrogen** and one progestogen, and unit doses contg. only one carrier. The trisequential delivery mode aims at compensating functional disorders caused by menopausal or pre-menopausal hypoestrogenism. Formulation of 1.5 mg 17.beta.-estradiol tablets and 2.5 mg nomegestrol acetate tablets are disclosed. The efficacy of tablets in **treatment** of hot flashes in menopausal women are reported.

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1/9/2003